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TASTE MASKING OF AMBROXOL HYDROCHLORIDE BY FORMULATING AND EVALUATION OF MICROSPERE BY USING SPRAY DRYER.

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ABSTRACT

These research work based on masking the taste of bitter drug. Ambroxol hydrochloride is selected as a suitable candidate for taste masking due to its bitter taste. The drug is use for all forms of Tracheobronchitis, Emphysema with bronchitis, Pneumoconiosis, Chronic inflammatory, Pulmonary condition, Bronchiectasis, bronchitis with Bronchospasm asthma, Silicosis.

The problem of bitter and obnoxious taste of drug in pediatric and geriatric formulations is a challenge to the pharmacist in the present scenario. In order to ensure patient compliance bitterness masking become essential. their are 9 methods of taste masking- coating of drug particles with inert agents, molecular complexes of drug with other chemicals, taste masking by formation of inclusion complexes, solid dispersion system, micro encapsulation, multiple emulsions, prodrugs, mass extrusion method, ion exchange resins.

Taste masking of Ambroxol hydrochloride done by using spray drying technique. Microparticals of Ambroxol hydrochloride were prepared in 1:3 (Ambroxol hydrochloride: HPMC and PVP) by using spray dryer. The percentage yield was found to be 28.23%. The encapsulation efficiency was found to be 50.48%. The in vitro drug release was found to be 70.39% and 76.56% in 0.1N HCL and PH 6.8 phosphate buffer solution.

Key words: Ambroxol hydrochloride, Hydroxypropyl methylcellulose (HPMC), Polyvinyl pyrrolidone (PVP), Carbomer, Sucrose, Spray drying, Taste masking.

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INTRODUCTION

In recent years, the use of a number of drugs including antibiotics which have undesirable tastes has been increasing. Although many drugs are widely administered parenterally, oral administration is more convenient and acceptable to patients. The problem of bitter and obnoxious taste of drug in pediatric and geriatric formulations is a challenge to the pharmacist in the present scenario. In order to ensure patient compliance bitterness masking becomes essential.

Diphenhydramine Hydrochloride is selected as a suitable candidate for taste masking due to its bitter taste. Taste masking can be done by using flavors, sweeteners and amino acids, also by using various techniques such as lipophillic vehicles, coating, inclusion complexation, ion exchange, effervescent agents, rheological modifications, solid dispersion systems, group alteration and prodrug approach, freeze drying process, wet spherical agglomeration technique and continuous multipurpose melt technology .

OBJECTIVE

The objective of the work is to develop efficient method to mask the bitter taste of ambroxol hydrochloride by using various polymer in ration and then formulate and evaluate the ambroxol hydrochloride microspere by combination with polymer using a spray dryer.

MATERIALS AND METHODS

Materials:

Ambroxol Hydrochloride was obtained from Maxhill MIDC Satpur Nashik as gift sample. Other AR grade chemicals were purchased from Merck laboratory and S. D. Fine-Chem Ltd. (India).

Experimental method:

Physicochemical method:

Organoleptic properties and description: The sample of ambroxol hydrochloride was studied for organoleptic character and found to be yellowish white, odorless and bitter crystalline powder.

Melting point: Capillary method was used and melting point was found to be- 235-240°C.

Method of analysis of drug candidate:

U V Spectroscopy: solutions were prepared in 0.1N HCL and 6.8 phosphate buffer and UV spectra were recorded in the range of 243.5nm.

Construction of Beer-Lambert's plot:

A stock solution of 1000µg/ml was prepared. Further dilution is made in the range of 10-60 µg/ml with water. The absorbance of each standard solution was recorded UV spectrometer, at the λmax 243.5 nm.

Preparation of ambroxol hydrochloride microparticles: (Trial batches)

Ambroxol hydrochloride and HPMC (1:3) :

500 mg drug dissolved in 25ml water and 1500mg HPMC was dissolve in 25ml water, both are mixed and report the result.

Ambroxol hydrochloride and PVP (1:3):

500mg drug and 1500mg of PVP was dissolved in water separately and mixed it. Report the result.

Ambroxol hydrochloride and carbopol(1:3):

500mg drug and 1500mg of carbopol was dissolved in water separately and mixed it. Report the result.

Ambroxol hydrochloride, PVP, HPMC and Sucrose (1:3:3:1):

500mg drug dissolved in 25ml water, 1500mg PVP, 1500mg HPMC and 500mg sucrose was dissolved in 50ml water, and report the result.

Ambroxol hydrochloride, PVP and HPMC(1:1:1):

500mg drug dissolved in 25ml water, 500mg of PVP and 500mg of HPMC dissolved in 25ml water, report the result.

Evaluation of microsperes: (ambroxol HCL:HPMC)

The prepared microsperes were evaluated for

Percent yield value- By using following formula-

$$\text{Percent yield value} = \frac{\text{Practical yield value}}{\text{Theoretical yield value}} \times 100 = \frac{7.9044}{28} \times 100 = 28.23\%$$

Encapsulation efficiency: By using following formula-

$$\text{Encapsulation efficiency} = \frac{\text{Estimated drug content}}{\text{Theoretical drug content}} \times 100 = \frac{3.5336}{7} \times 100 = 50.48\%$$

In vitro drug release study from ambroxol hydrochloride microsperes:

Micropartical equivalent to 30mg filled in capsule and invitro drug release studied using USP apparatus И with 900ml disso. Media at 37.5±0.1°C for 2 hr at 50 rpm. 10ml of sample was withdrawn after every half hr. and replaced with an equal volume of fresh medium. Dissolution data for microparticles in different medium like 0.1N HCL and ph 6.8 phosphate buffers are reported at 243.5 nm.

Gustatory sensation test :

Gustatory sensation test was carried out according to the method of Shah et al..

Ten volunteers participated in the sensory test. One gram of microparticles was dispersed in 100 ml of water for 15 s. Ambroxol HCL was used as a control. Immediately after preparation, each volunteer held about 1 ml of the dispersion in the mouth for 30 s. After expectoration, the bitterness level was recorded. A numerical scale was used with the following values: 0 – tasteless, 0.5 to 1 – slightly bitter, 1to 1.5 – slightly to moderately bitter, 2 – moderately bitter, 2.5 – moderately to strongly bitter, 3+ – very strongly bitter. The threshold of bitterness of microparticles was determined as the point at which most volunteers described the taste as bitter or slightly biter.

RESULTS AND DISCUSSION :

Table 1: Formulations :(trial)

Sr. no.	Drug and polymer ration	Result obtained
1	Drug and HPMC(1:3)	Taste masked.
2	Drug and PVP(1:3)	Taste masked.
3	Drug and Carbomer(1:3)	Taste not masked.
4	Drug,PVP, HPMC and Sucrose(1:3:3:1)	Taste not masked.
5	Drug, PVP and HPMC	Taste not masked.

Table 2: Absorbance – concentration data for standard calibration curve of ambroxol hydrochloride in water.

Conc.(µg/ml)	Absorbance	Equation of line and correlation coefficient
10	0.269	
20	0.586	
30	0.833	
40	1.136	Y = 0.028X + 0.0024
50	1.382	R^2 = 0.9989
60	1.692	

Table 3: In-vitro drug release study. (Drug: HPMC):

Time(min)	Cumulative % release	
	0.1 N HCL	PH 6.8 phosphate buffer
30	25	30
60	30.05	45
90	50.36	60
120	70.39	76.56

Figure 1: Beer-lambert's plot of ambroxol hydrochloride in distilled water.

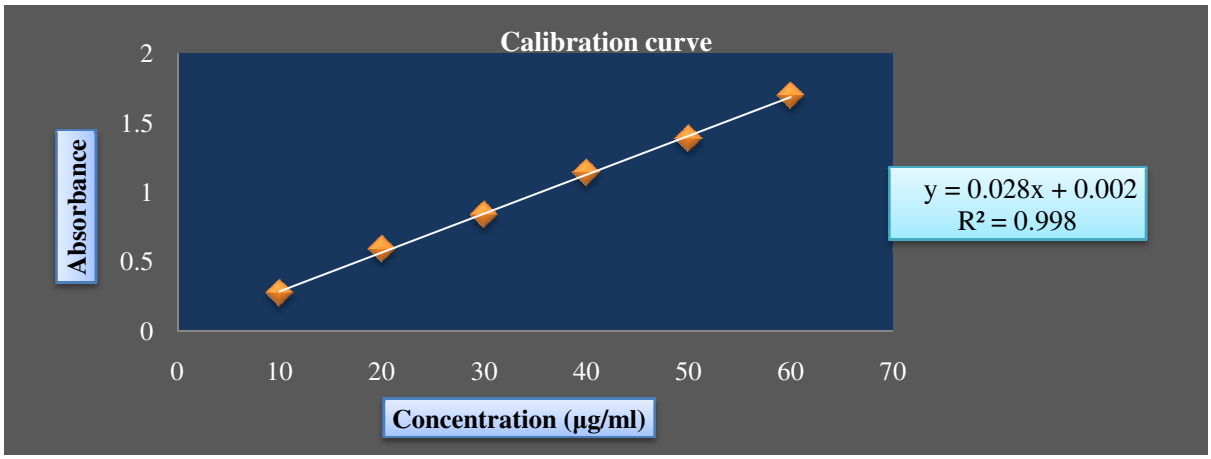


Figure 2: Dissolution profile of microparticles in 0.1N Hcl (Percentage drug released versus time in min.).

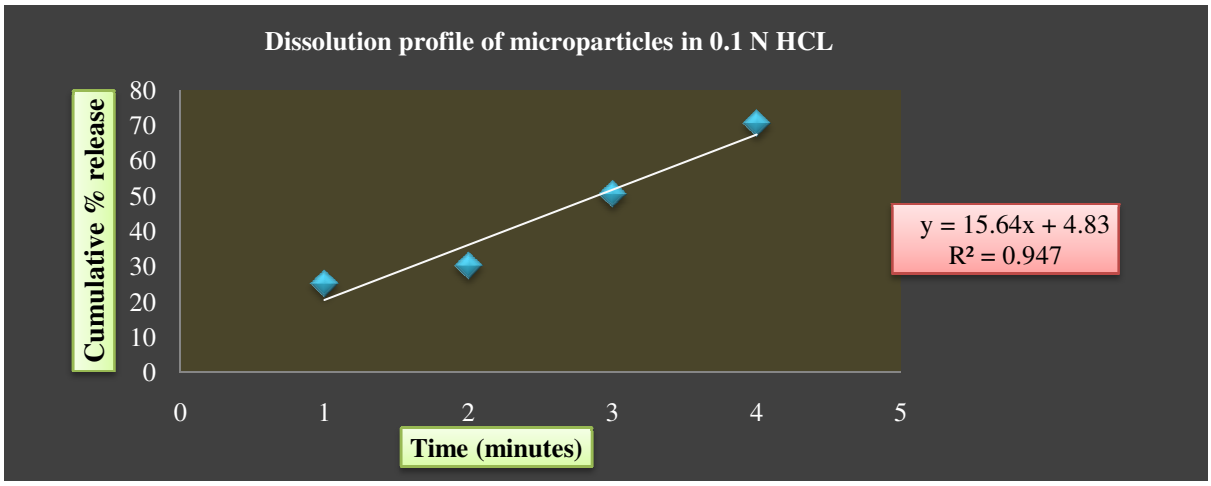
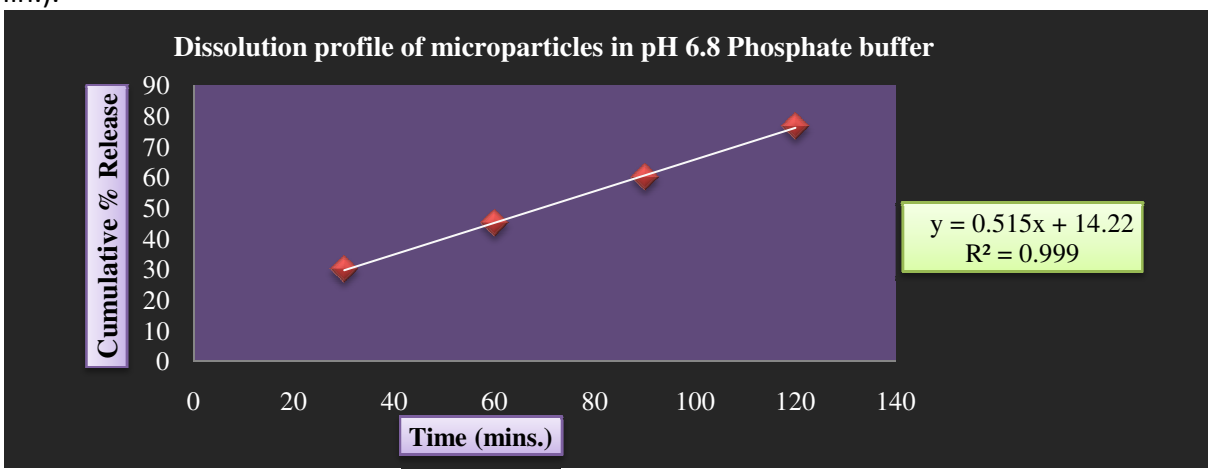


Figure 3: Dissolution profile of microparticles in Ph 6.8 phosphate buffer (percentage drug released verses time in min.).



DISCUSSION

The taste of ambroxol hydrochloride was masked by HPMC and PVP but some sticky problem may arise with PVP, so that we choose an HPMC combination and get a result. And the other combination fail to mask and having an hygroscopic nature may degrade the drug. The % yield was found to be 28.23%. The encapsulation efficiency

was found to be 50.48%. The in vivo drug release was found to be 70.39% and 76.56% in 0.1N HCL and PH 6.8 phosphate buffer solution.

CONCLUSION

From above experimental data, it was concluded that the ambroxol HCL is very much bitter drug and taste is masked by formulating various combination of drug and polymer HPMC. And drug release most found with HPMC. Other polymer not mask the taste of drug and because of hygroscopic property may degrade the drug.

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