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FORMULATION AND STABILIZATION OF BROMHEXINE HYDROCHLORIDE ORAL SYRUP

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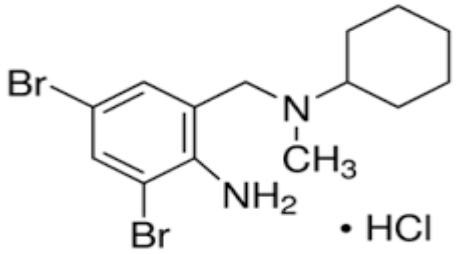
Abstract
Formulation scientist in the present pharmaceutical industry faced a lot of problems regarding stability of the liquid formulation as some of the active compounds having some problem in dissolving, showing precipitation when exposed to stability studies. In the present study performed on Bromhexine orals syrup as having stability issue that it becomes turbid exposure to a accelerated stability studies so to overcome this problem Malic acid was used to stable this formulation.

Keywords: - Formulation, Physicochemical properties, Accelerated Stability study.

Introduction

Stability in pharmaceutical formulation is critical as well as basic parameters. The oral use of liquid pharmaceuticals has generally been justified on the basis of ease of administration to those individuals who have difficulty in swallowing solid dosage forms. With rare exceptions, a drug must be in solution in order to be absorbed. A drug administered in solution is immediately available for absorption, and in most cases, is more rapidly and efficiently absorbed than the same amount of drug administered in a tablet or capsule. [1, 2]

Bromhexine is an oral mucolytic agent with a low level of associated toxicity. Bromhexine acts on the mucus at the formative stages in the glands, within the mucus-secreting cells. Bromhexine disrupts the structure of acid mucopolysaccharide fibres in mucoid sputum and produces less viscous mucus, which is easier to expectorate. [3]



Human skin Figure No 1: - Chemical Structure of Bromhexine Hydrochloride

Materials and Methods

Bromhexine Hydrochloride was procured as a gift sample from Ratchet Lab, Limited. Other excipients were purchased from S.D fine chemicals.

Methods

1. Preparation of Base: -

- Take 30 ml Purified water. Add sugar and heat up to 80-90 degree with continuous stirring until get clear and cool up to 40 degree.
- Add Sorbitol and Glycerin into step no 1 with continuous stirring to get a clear solution.
- Take 100ml purified water and dissolve Sodium methyl paraben, Sodium propyl paraben, Sucralose with continuous stirring to get a clear solution and add into step no 1.

2. Preparation of Drug Solution: -

- Take Propylene Glycol and heat up to 50 Degree with continuous stirring until get clear. Cool the solution to room temperature.
- Dissolve Malic Acid in Purified water and add in to step no 1 with continuous stirring and check the clarity of the solution.

3. Add Step no 2.0 into step no 1.0 with continuous stirring and check the clarity of the solution.

4. Addition of Colors:- Dissolve Colour into purified water and add into step no 1 with continuous stirring and add into step no 1.

5. Addition of Flavors: - Add Flavour into Step no 1

with continuous stirring.

6. Adjustment and Volume make up: - Dissolve Malic acid in purified water and adjust pH in the range of 4.0-4.5 and volume was making up with purified water.

Formulation of Stabilized Syrup

A series of formulations were prepared as given in table 1 with various concentrations of excipients and were evaluated for stability, pH, Clarity. F1 to F4 formulation were formulated by using different excipients.

Table No 1: - Formulation of Stabilized Syrup

S. No.	Ingredients	F1	F2	F3	F4
1.	Bromhexine HCL	0.80	0.80	0.80	0.80
2.	Sodium methyl paraben	1.00	1.00	1.00	1.00
3.	Sodium propyl paraben	0.10	0.10	0.10	0.10
4.	Sodium Benzoate	-	2.00	-	-
5.	Sugar	400.00	600.00	300.00	500.00
6.	Sorbitol solution 70%	30.00	-	50.00	50.00
7.	Citric Acid Monohydrate	3.00	3.00	-	3.00
8.	Propylene glycol	125.00	120.00	70.00	120.00
9.	Glycerin	30.00	30.00	30.00	30.00
10.	Sucralose	2.00	2.00	2.00	2.00
11.	Malic Acid	-	-	4.0	-
12.	Colour: Ponceau 4R (supra)				
13.	Flavour Sweet Orange	2.40	2.4	2.4	2.4

Use of Excipients in Formulation

Different type of excipients were use in this formulation so to explore the use of the excipients explained in the tabular as shown in table no 2.

Table No 2: - Use of excipients in Formulation.

S. No	Ingredients	Quantity (1 L)	Use
1.	Bromhexine HCL	0.80	Active
2.	Sodium methyl paraben	1.00	Preservative
3.	Sodium propyl paraben	0.10	Preservative
4.	Sugar	300.00	Base
5.	Sorbitol solution 70%	50.00	Base
6.	Propylene glycol	70.00	Solubilizing Agent
7.	Glycerin	30.00	Stabilizing Agent
8.	Sucralose	2.00	Sweetening Agent
9.	Malic Acid	4.0	Acidifier
10.	Colour: Ponceau 4R (supra)		Coloring Agent
11.	Flavour Sweet Orange	2.4	Flavoring Agent

Table No 3: - Result of physically parameter of developed stabilized syrup

S. No	Physicochemical Parameters	Range	Observed Value
1	Clarity	Clear Solution	Complies
2	Colour	Light orange color	Complies
3	Odor	Orange sweet	Complies
4	Taste	Slightly bitter	Complies
5	pH	4.0-4.5	4.3

Table No 4: - Stability studies through Physicochemical Parameters

Formulation Code	Study Type	Temperature & RH	Physicochemical Parameters				
			Clarity	Colour	Odor	Taste	pH
F1	Acc	40 ± 2 °C and 75 ± 5% RH	Turbidity	Light orange color	Orange sweet	Slightly bitter	5.0
F2	Acc	40 ± 2 °C and 75 ± 5% RH	Turbidity	Light orange color	Orange sweet	Slightly bitter	4.8
F3	Acc	40 ± 2 °C and 75 ± 5% RH	Clear Solution	Light orange color	Orange sweet	Slightly bitter	4.4
F4	Acc	40 ± 2 °C and 75 ± 5% RH	Turbidity	Light orange color	Orange sweet	Slightly bitter	4.7

Evaluation of Developed Oral Stabilized Formulation

1. **Color examination**: - Five ml final syrup was taken into watch glasses and placed against white back ground in white tube light. It was observed for its color by naked eye.
2. **Odor examination**: - Two ml of final syrup was smelled individually. The time interval among two smelling was kept 2 minutes to nullify the effect of previous smelling.
3. **Taste examination**: - A pinch of final syrup was taken and examined for its taste on taste buds of the tongue.
4. **Determination of pH**: - pH of the suspension was determined by the use of Metler Toledo pH meter.

Accelerated Stability Study

F1 to F4 oral syrup formulation were packed in 100 ml Amber color pet bottle. The packed bottles were placed in stability chamber maintained at 40 + 2 °C and 75 + 5% RH for 3 month. Samples were collected at days 0, 30, 60 and 90. The analyses comprised chemical testing of quantifiable parameters, which could possibly change during storage, such as Colour, pH, drug contents, taste and odor.

Result

In the past it was the practice in many pharmaceutical manufacturing companies to evaluate the stability of pharmaceutical preparations by observing them for a year or more, corresponding to the normal time that they would remain in stock and in use. Such approach was time consuming. Now a day's Accelerated stability studies are used by most of the pharmaceuticals for stability evaluation of all types of formulations. [4] In four formulation from F1 to F4. F3 will be the best formulation that observed after accelerated study on the basis of clarity, odor, taste and pH.

Conclusion

In conclusion, stabilized formulation of Bromhexine syrup prepared in the laboratory scale may be used as a stable liquid dosage form and the results of the accelerated stability study will help in justifying the stability of the formulation in future.

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