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Formulation and Development of Ambroxol Hydrochloride Syrup.

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ABSTRACT: The main objective to present investigation to develop ambroxol hydrochloride syrup. It evaluated for all physicochemical properties and dissolution test. From that syrup SI shows high dissolution compared to other formulations maintain for good stability of ambroxol hydrochloride syrup.

Key words: Syrup, drug components, ambroxol dissolution physiochemical properties.

I. INTRODUCTION:

Syrups are concentratedaqueous preparations of sugar or sugar substance's with or without flavouring agents and medicinal substances. It is in the form of thick liquid. There are various or different types of syrups that are used for various purposes and in the formulation of syrups different components are used like sugars, flavours, colours preservatives.

Types of syrups: The are three types of syrups are there, they are

- Simple syrup
- Medicated syrup
- Flavoured

Simple syrup: It is a concentrated viscous aqueous solution of sucrose/sugar substitute with or without flavouring agents and medicinal substances in purified water (66.6% w/w).

Medicated syrup: Medicated syrup contains the medicinal agents and the medicinal substances and shoes the therapeutic effect is called as medicated syrup. E.g., Ambroxol HCL.

Flavoured syrup: The flavoured syrups are used to increase the patient acceptability. These syrups contain the flavouring agents. E.g., Lemon syrup orange syrup cherry syrup etc.....

Advantages

- ✓ Used for treatment of throat and mouth infections.
- ✓ It is easy to swallow thereafter easier for children and old age people.
- ✓ It is simple and fast to formulate.
- ✓ It can be administered easily and easily available.
- ✓ It is homogenous thereafter give uniform dose then suspension or emulsion which need shaking.

Disadvantages

- ✓ Patient uncomfortable.
- ✓ Require assistant or nurse for administration.
- ✓ Alcoholic and hydro alcoholic solutions may produce irritation to skin.
- ✓ Drug solubility often reduced in solution.
- ✓ They are bulky, so difficult to transport and store.
- ✓ Other major sign for drug stability are colour change, preparation and microbial growth.

II. MATERIALS AND METHODS

Name of the materials	Manufacturer supplier	Function
Ambroxol HCL	Koraer India-koraesina	Active ingredient
Sucrose	Dharani sugar Pvt Ltd TN	Sweetener
Sodium saccharin	China Pvt Ltd Vardhman& co Chennai	Sweetener
Sucralose	Tate & lyte Pvt Ltd KP Manis global Co-Chennai	Sweetener
Propylene glycol I. P	Salicylate Pvt Ltd chemicals Hyderabad	Preservative
Glycerine	Godrej industries Ltd Mumbai	Viscosity binder
Hydroxy propyl cellulose	Laffano detro chemicals Ltd	Viscosity binder
Menthol	Hindustan Pvt Ltd vardhaman co Chennai	Flavouring agent

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Citric acid	Sunil chemicals	Acidulate
Sodium citrate	Sunil chemicals	Buffering agent
Flavouring oil	Aromatics India Pvt Ltd Daman	Flavouring agents

Table No.1 Materials used in the study.

Reason for formulating ambroxol hydrochloride syrup: Ambroxol is used for the treatment of sore throat owing to its analgesic effect, and it generally prepared into syrup formulation so that it acts and has a long-lasting analgesic effect of at least 3 hours. It clears congestion in the treatment of respiratory diseases which have thick phlegm

Equipment's used

S.NO	Instrument/Equipment's	Manufacturer/Supplier
1	Electronic weighing balance	Shimadzu Japan
2	Viscometer	Lab equipment MMC Pvt Ltd Chennai
3	PH meter	Digi-sun electronics Hyderabad
4	Dissolution test apparatus	Veego (UDA-60)
5	UV visible spectrophotometers	UV pharma 1700 Shimadzu
6	HPLC	HPLC-LC 99 Shimadzu Japan
7	TLC	Lab equipment MMC Pvt Ltd Chennai
8	Water bath	Lab equipment MMC Pvt Ltd Chennai
9	Humidity chamber	Lab equipment MMC Pvt Ltd Chennai
10	Hot air oven	Lab equipment MMC Pvt Ltd Chennai
11	Melting point	Lab equipment MMC Pvt Ltd Chennai
12	FTIR	Lab equipment MMC Pvt Ltd Chennai

Table No.2 Equipment's used in the study.

Formulation and development

Ingredients	S1	S2	S3	S4	S5
Ambroxol HCL(g)	3	3	3	3	3
Propylene glycol (g)	50	100	150	50	50
Glycerine (g)	50	100	150	50	50
Sucralose (g)	1.5	11.5	1.5	-	-
Sodium saccharin (g)	-	-	-	1	-
Sucrose (g)	-	-	-	-	250
HPC (g)	1	1	1	1	1
Menthol (g)	0.5	0.5	0.5	0.5	0.5
Citric acid (g)	1	1	1	1	1
Sodium citrate (g)	1	1	1	1	1
DM water q.s	Make up to 500ml	Make up to 500 ml	Make up to 500ml	Make up to 500ml	Make up to 500ml

Table No.3 Compositions used in the formulation of syrups.

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Procedure

Step 1

Propylene glycol is mixed with the active pharmaceutical ingredient Ambroxol hydrochloride.

Step 2

To the above mixture hydroxypropyl cellulose and glycerine were added and mixed well using 100ml of water.

Step 3

The resultant mixture was stored in a well closed container for 20 hours or overnight at room temperature.

Step 4

0.5 ml of flavouring agent was then added and the PH was measuredstudies.

Step 5

The PH was adjusted to PH to PH by using citric acid solution and sodium citrate solution.

Step 6

After 20 hours or overnight store sucralose or sucrose or sodium saccharin sodium was added and the volume was made up to 500ml using distilled water.

Preformulating studies of ambroxol - hydrochloride

It is one of the important prerequisitesin development of any drug delivery.Preformulation studies were performed on the drug. Which included melting point determination, solubility and compatibility studies.

Determination of melting point: Melting point of Ambroxol HCL was determined by capillary method.Fine powder of Ambroxol hydrochloride was filled in glass capillary tube (previously sealed on one end). The capillary tube tied to thermometer and the thermometer was placed in flam. The powder at what temperature it will melt was noticed.

Solubility: 1mg Ambroxol HCL was dissolved in100ml of different solvents like water methylene chloride, ethanol and ether separately and was tested for solubility as per BP 2000.

Determination of ג max: Asolution of ambroxol hydrochloride containing the concentration 10µg/ml was prepared in 0.1N HCL and UV spectrum was taken using Shimadzu UV double beam spectrophotometer. The solution was scanned in the range of 200 to 400nm.

Preparation of standard stocksolution of Ambroxol HCL: 30mg of Ambroxol HCL was dissolved in 100ml of 0.1N HCL. Aliquot of stock solution was further diluted by using the same solvent to obtain concentration range from 80mcg/ml-120mcg/ml. The absorbance of the solution was measured at 301nm using UV visible spectrophotometer.

Preparation of 0.1N Hydrochloric acid: 8.5ml of the Ambroxol Hydrochloric acid was taken and dissolved in water and make up to1000ml to get 0.1N hydrochloric acid. Drug excipients compatibility study (25) compatibility studies were carried out to study the possible interactions between Ambroxol HCL and other inactive ingredients. The compatibility studies were carried out an aim to select a suitable excipient for a stable and best formulation. Blend of drug with excipient in suitable ratios were filled in a glass vial for exposing to 400c/75% RH and observed for physical changes.

III. RESULTS AND DISCUSSION

Melting point determination: Melting point of Ambroxol HCL was found to be 237ºC.

Stability

S.NO	Solvents	Solubility
1	Water	Sparingly soluble
2	Methylene chloride	Slightly soluble
3	Ethanol	Soluble
4	Ether	Partially soluble

Table No.4 Solubility of Ambroxol HCL in various solvents.

Absorbance data for thecalibration curve of Ambroxol HCL in 0.1N HCL

S.NO	TIME (MIN)	S1	S2	S3	S4	S5	Market Sample syrup	Market sample tablet
1	15	105.03	86.32	84.07	86.32	86.04	84.07	58.11
2	30	107.67	87.84	84.54	87.84	86.06	86.04	68.51
3	45	111.37	89.36	88.04	88.04	88.37	86.06	80.08

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4	60	113.48	91.87	88.37	89.36	88.40	88.40	86.54yeah where is the valley

Table No.5 Absorbance data for the calibration curve of Ambroxol HCL in0.IN HCL.

IV. DISCUSSION:

Melting point of Ambroxol HCL was found to be 237C.Ambroxol was sparingly soluble in water, slightly soluble in methylene chloride and soluble in ethanol partially insoluble in ether.From the UV spectra of the drug, it was confirmed that the drug is having maximum absorption at the wavelength of 308nm.It was found that the solution of Ambroxol HCL in 0.1N HCL shows linearity.In absorbance concentration of 60-140mcg/ml and obeys Beers Lamberts law.Syrups were formulated in different combinations S1,S2,S3,S4,&S5.Compatibility studies were done by FR-IR study and it was found that the excipients are compatible with API.Different parameters like pH, specific gravity, viscosity and assay were done for all the formulations and all the values were within the limit.The formulation was studied for the presence of microbes. All the values obtained were within the limit. Pathogenic organisms were absent.All the formulations were tested for related substances by HCL method and no impurities were obtained during the study.From the release profile the similarity factor was calculated within the marketed syrup solution.The f2 value of S3 formulation was found to be higher (92.24) when compared to other formulations.All the formulations were kept for stability study and the parameters such as PH, specific gravity, viscosity, related substance and assay were found to be within the limit.10-30 bacterial colonies were formed in each formulation which are kept for stability study in accelerated condition and it was within the limit.There were no countable colonies observed in the accelerated conditions.

V. CONCLUSION

From the study which was carried out it was concluded that:

The S3 batch was selected as the best formulation based on thevarious evaluation'sstudies. The formulation S3 was compared with a marketed sample of Ambroxol HCL syrup and tablet it was found that the drug release from the formulated syrup matches the drug release profile of the marketed syrup sample.The drug release from the formulated syrup was higher when compared with that of the marketed tablet sample.Stability studies also concluded that the drug release profile are other parameters did not alter significantly after the accelerated stability studies. Hence stable Ambroxol Hydrochloride syrup which has a similarity factor of 93 with the marketed syrup was formulated successfully using sucralose as the sweetening agent. Further work can be continued to make formulations with suitable excipients that can prevent crystallization and to Impart latest technique to mask the bitter taste of the drug.

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