Study on usage and evaluation of stevioside as sweetening agent in salbutamol sulphate and Bromhexine hydrochloride syrups

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Citation

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Abstract

Stevioside is an intense sweetener ideally suited for liquid oral dosage forms such as Syrups, Dry syrups and suspensions. In the study syrups were prepared using stevioside as sweetener in 0.5 and 1% w/v concentration, salbutamol sulphate and Bromhexine hydrochloride in combination as model drugs. The usage of stevioside can offer many advantages to patients suffering from Diabetes, Phenylketonurea and calorie conscious, ranging from pediatrics to geriatrics. If the sweetener is soluble in the solvent, concentration of stevioside required is less i.e. up to 0.5% w/v. Formulated liquid oral dosage forms were stable at room temperature and showed good sweetness and palatability and were evaluated for drug content, viscosity, pH, and compatibility studies. Evaluation of the sweeteners and palatability was done using a panel of trained volunteers and it was observed that concentration of 0.5% w/v of Stevioside showed good sweetness and palatability.

INTRODUCTION

Salbutamol sulphate and Bromhexine hydrochloride is an orally administered Bronchodilator and Mucolytic agent respectively. Preferably given in sinusitis, productive cough and other allergic conditions in combination therapy to overcome the symptoms related. Salbutamol sulphate and Bromhexine hydrochloride can be administered to all range of patients ranging from pediatrics to geriatrics in liquid oral dosages [1,2] .The syrups which are available in the market either they are made up synthetic or semisynhtetic origin and have reported to cause many causalities in patients, and the syrups of sucrose may contraindicated in patients suffering from diabetes, phenylketonurea and calorie conscious. So usage of these types of sweetening agents in formulations have made their use restricted to a narrow range of patients on the basis of their above mentioned pathological conditions [3] . Though many types of syrup of Salbutamol sulphate and Bromhexine hydrochloride are available commercially, no work was reported on the pharmaceutical formulations aspects using stevioside as sweetener. Among the various methods of preparations of syrups, making Solutions of ingredients with the aid of heat is an industrially accepted method and it is well practiced in laboratory scale also. Among the various sweeteners available, stevioside can also be used as an alternative for sucrose and synthetics. Stevioside has to receive increased acceptability and application in pharmaceutical formulations in coming years due to approval by various regulatory agencies. Stevioside is a Diterpine glycoside extracted from the plant Stevia reboudiana [4] , it is white or creamy-white coloured free flowing powder with intense sweet taste. Soluble in cold water, ethanol, methanol and ether. It is generally regarded as a non-toxic and non-irritant material .It has been accepted by WHO and it is added in Generally Recognized as Safe (GRAS) class. It has not shown any interaction with the drug and analyzed for the results of drug content, viscosity, stability and palatability and are in acceptable range. In the present work syrups of Salbutamol sulphate and Bromhexine hydrochloride were formulated and evaluated with an objective of enhancing the sweetness and palatability.

MATERIALS

Salbutamol sulphate and Bromhexine hydrochloride were gift sample from M/s Crystal Pharmaceutical Ltd, Hubli and Elvina Pharmaceutical Ltd. Kotur. Propylene glycol, Menthol was gift samples from S.D. Fine Chem. Ltd, were gift samples from S.D. Fine Chem. Ltd; Sodium hydroxide was gift sample from Ranbaxy fine chem. Ltd; Colour Erythrosine was gift sample from M/s Elvina Pharmaceutical

Ltd; Banana flavour and Saffron essence were gift samples from DFF Ltd, Bangalore. Chloroform water was in-house preparation, Stevioside was gift sample from M/s Qufu haigan stevia pvt.ltd Quingado, China.

METHOD

Salbutamol sulphate and Bromhexine hydrochloride

Preparation of syrup [5] :(f_1 and f_2)

Add about 40mL of D.M water to the beaker and heat it to about 70?C , dissolve required quantities of stevioside powder by stirring , add propyl paraben and methyl paraben stir at 300rpm to result clear solution, filter this base and cool to room temperature. Add sorbitol under stirring till it gets mixed to the solution. Salbutamol sulphate is added to the water and this solution is added to the base mixture. Warm, PEG-400 to 65?C and dissolve Bromhexine hydrochloride in it. Transfer this solution to the base mixture. Dissolve Citric acid in water and add to the above. Dissolve menthol in rose flavour and is added to the base mixture.

Make up the volume with D.M water to 100mL and filtered finally.

Figure 1

Sl.no	Formulation Ingredients	Quantity for 2000Liters	QuantityFor100mL
1	salbutamol sulphate	0.48kg	0.024gms
2	Bromhexinehydrochloride	0.8kg	0.040gms
3	Menthol	0.5kg	0.025gms
4	Propyl paraben	0.20kg	0.01gms
5	Propyl paraben	2kg	0.1gms
6	Sorbitol	200Kg	10gm
7	PEG-400	130.0kg	6.5gm
8	Citric acid	1.2kg	0.06gm
9	Rose flavour	2.5L	0.125mL
10	Demineralised water to	2000L	100mL qs.
11	Stevioside sweetener	0.5 and 1%	0.5 and 1%

The evaluation parameters applied to prepared syrups are Appearance, pH, Viscosity was measured by Brookefield viscometer DV 2P, Taste evaluation and stability studies were carried out. Salbutamol sulphate and Bromhexine hydrochloride content estimated by a reported spectrophotometric method [6] . The interaction study was carried for Stevioside and Salbutamol sulphate and Bromhexine hydrochloride individually and in combination using FTIR.

Taste evaluation [7,8] : The Tasting panel consisting of 10 trained panelists, consisting of 5 males and 5 females of age group 20-30 years, who were instructed to keep the sample to be tasted in oral cavity for about 30 seconds and is expectorated, each panelist is advised to taste it thrice in an hour to get mean reading of the same. After every expectoration the members are asked to rinse oral cavity with sufficient water to avoid overlapping of tasting sense of tongue. On the basis of their mouth feel effect, felt by them they are asked to rate the sample from 0 to 6. Points are allotted for each taste, like Sweet, Bitter, Palatable and its flavour. The points which are obtained are made to add to get the total of each parameter to decide its acceptance by the panel members. The sample of liquid oral solution taken for study is about 5mL.

RESULTS AND DISCUSSIONS

Syrup could be prepared by small rise in temperature method employing Stevioside as sweetener and D.M.water as vehicle. Salbutamol sulphate and Bromhexine hydrochloride content, Appearance, pH, Viscosity, and stability studies are given in table 2 and Taste evaluation is given in table 3.

Figure 2

Table 2

Formulation code	Colour	Odour	pH	Viscosity	Drug content at Zero day	Stability studies For one week
F_1	Light yellow	Rose flavour	3.7±0.2	116 cps	S*1.9164mg/10ml B*3.9006mg/10ml	**S*1.9158mg/10ml** B*3.9006mg/10ml
F_2	Light yellow	Rose flavour	3.5±0.2	112 cps	S*1.9294mg/10ml B*3.8570mg/10ml	S*1.9287mg/10ml B*3.8567mg/10ml

S* Salbutamol sulphate, B* Bromhexine hydrochloride

Figure 3

Table 3: Tasting panel Score card for formulation F and F

	F_1				F_2			
Volunteer No.	Sweet	Bitter	Palatable	Flavour	Sweet	Bitter	Palatable	Flavour
V1	4	2.5	5	5	3.5	4	4	4
V2	4.5	2.5	4.5	4.5	4	3.5	4	4
V3	4.5	3	4.5	4.5	4	2.5	4.5	3.5
V4	4.5	2.5	4.5	5	4.5	2.5	4.5	4.5
V5	5	3	4.5	4.5	3.5	2.5	4	4
V6	4.5	2.5	4.5	4	4.5	3.5	4.5	4.5
V7	4.5	3	5.5	4.5	3	3	4.5	3.5
V8	4	2.5	4.5	5	3.5	3.5	3.5	3.5
V9	4.5	3	5	5	4	3.5	4	4
V10	4	3.5	4.5	4.5	4	2.5	4.5	4
Total	44.5	28.0	47.0	46.5	38.5	31.0	39.0	39.5

The results obtained are in acceptable range and the tasting panel score card has given some information on total points scored and it was shown maximum points by F_1 i.e. by 0.5% w/v of Stevioside when compared to F_2 i.e. 1% w/v of

Stevioside sweetener.

Figure 4

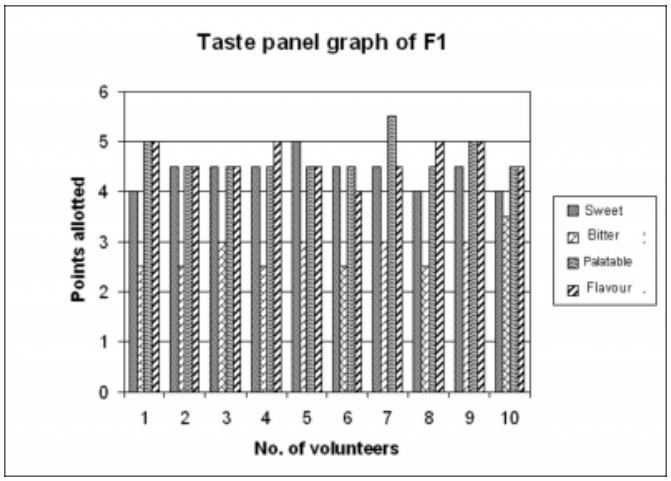
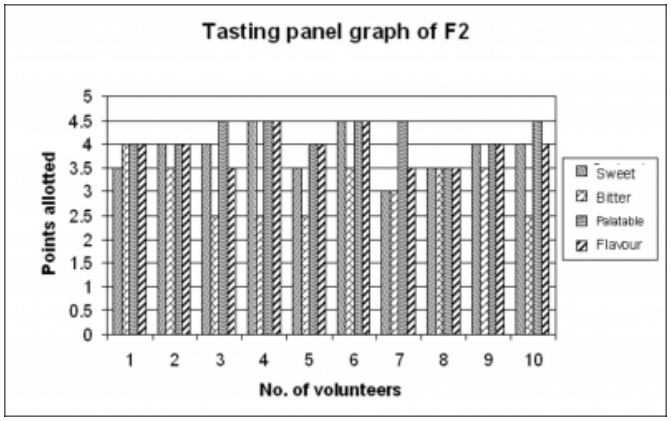


Figure 5



CONCLUSIONS

- Formulations F1 with stevioside at 0.5% w/v showed good sweetness and palatability due to its intense sweetness.
- The solubility of sweetener decides the concentration to be used if it is soluble then it may require in small concentrations i.e. is up to 0.5% w/v or it may be used above this concentrations if its solubility is very less in the vehicle used for the preparations.
- The formulated liquid oral dosage forms prepared with stevioside as sweetener showed good physical properties like appearance, viscosity, and odour.
- Various evaluation parameters like organoleptic properties, viscosity, drug content and stability values in all formulations were within specified limits.
- By considering all the above parameters it can concluded that stevioside can be used as an alternative sweetener in liquid oral dosage forms.

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