FORMULATION AND IN-VITRO EVALUATION OF TERBUTALINE SULPHATE SUSTAINED RELEASE TABLETS

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ABSTRACT

Sustain release formulation maintain a constant level plasma concentration of drug so that multiple and night dosing can be avoided. Terbutaline sulphate is a β_2 stimulant drug which is having a very short half life of less than 4 hours. It is available in conventional dosage form in thrice a day formulation. Being half life less there is always a need for dosing frequency. Decreasing dosing frequency will increase the patient compliance for asthmatic patients and thus avoiding dosing at odd hours. Terbutaline sulphate is available in market in different immediate release dosage forms. After some time plasma concentration level decreases below MEC. So the necessity of producing the drug in sustained release formulation. So an attempt is made to formulate terbutaline sulphate in sustained release formulation with different concentrations of HPMC K15 and HPMC K4M polymers so that it can provide effective drug release up to 12 hours. The powder blend is subjected to pre compressional parameters. The prepared tablets were subjected to post compressional parameters. The results of the present study showed that the polymer ratio used in the formulation F5 showed enhanced result and released the drug up to 12 hours with 99 % drug release.

Key words: Asthma,Terbutaline sulphate, β2-adrenergicagonists, Sustained release

INTRODUCTION

Asthma is the predeposition to chronic inflammation of the lungs in which the bronchi are narrowed. It is most common in childhood and occurs in approximately 10% of the pediatric population(S.P. Vyas et.al,2004). People with asthma have extra sensitive or hyper responsive airways. The airways react by narrowing or obstructing when they become irritated. There are two factors that provoke asthma. Triggers result in tightening of the airways and other would be inflammation of the airways due to allergens (Harish NM, 2011). Probably 75-80% of young asthmatics are allergic. It affects children varying degree from very mild to very severe. There is a general trend of increased deaths and hospitalization from asthma recorded in an entire all the industrialized countries of the world (Ranabir Chandaa, 2010, Ibrahim Khattab, 2009).Terbutalinesulphate is an effective broncho dilator and relatively short acting β2-adrenergicagonistsused in the treatment of bronchial asthma, chronic bronchitis and emphysema. It has shorter biological half life of 3-4hours.The usual does of TBS for oral adults is 5mg taken every 6 hours 3 times a day. In children 12 to 15 year age the used does is 2.5 mg 3 times a daily.Terbutaline is incompletely absorbed from the GIT and also subject to extensive first pass metabolism by sulphate conjugation in the liver and possibly by the gut wall. However due to short biological half life and low bioavailability of the drug high frequency dosing is necessary for the effective therapy (NandvishalV.Deore et.al,1012). Its short biological half life and thus frequent administration create necessity to development of long acting formulation is desirable to improve not only the treatment of lung disorder but also the patients compliance. In the present investigation it was tried to develop long acting formulation of terbutalinesulphate to improve itself.Attempt was made to prepare sustained release tablets of terbutalinesulphate using different concentrations of sustained release polymers.(Naresh B.Rajgor, 2010)

MATERIALS AND METHODS

Terbutaline sulphate was obtained from Darwin laboratories,Vijayawada,HPMC K15and HPMC K 4Mwas obtained from Coloron Asia Pvt.Ltd,Goa, Ethyl cellulose was obtained from Loba Cheme Pvt.Ltd ,Mumbai ,Iso propyl alcoholwas obtained from Finar reagents,Ahmedabad, lactosewas obtained from Loba cheme pvt.ltd,Mumbai, PVP K 30was obtained from Qualikens,Vadodara, Magnesium stearate and Talc was obtained from Sd.Fine Chemicals Ltd.Mumbai.

Preformulation studies: The powder blend was subjected to preformulation studies like bulk density, tapped density,Angle of repose, Carr's compressibility index,Hausner's ratio.(RaghavendraRao, 2012)

Drug-excipient Compatability Study: The IR absorption spectra of the pure drug and with different excipients were taken in the range of 4000-450 cm^{-1} using KBr disc method. (Sahin, 2009)

Formulation of 7.5mg Terbutalinesulphate sustained release tablets: Tablets containing 7.5 mg of Terbutalinesulphatewere prepared with a total tablet weight of 120 mg considering the Preformulation studies and the literature survey, the excipients were selected and an attempt was made to produce sustained release tablets maintaining the basic tablet properties.

Procedure: Granules were prepared by using wet granulation technique. Ingredients were weighed and taken in to motor. Finally the active ingredient was mixed homogeneously according to geometric proportions. Selected polymers are added. All the ingredients are made into a mass with alcoholic 3% solution of PVP K30.

The coherent mass was thoroughly sieved through 16 mesh and then dried in hot air oven at 50ºC for 45 min. The dried granules were passed through sieve no 20 to get uniform granules. To this calculated amount of Magnesium Stearate and Talc were added as a lubricant. Then the prepared granules were evaluated in the following parameters bulkdensity, tapped density, angle of repose, compressibility index and Hausner's ratio.

Post formulation studies: The f**o**rmulated tablets were subjected to post formulation parameters like Thickness, Hardness, Weight variation, Friability(Harish NM et.al,2011).Invitro dissolution and stability studies.(USP,2010)

RESULTS AND DISCUSSION

Drug-excipients compatibility studies by observing physical appearance: The pure drug and along with formulation excipients were subjected to compatibilitystudies and studies were carried out by mixing definite proportions of drug andexcipients and kept on glass vials which are stored in desiccator for one month.

Drug- Excipients compatibility studies by Infrared spectroscopy: Infrared spectra were recorded on a Fourier transform Infrared (FTIR) spectrophotometer using KBr dispersion method. All samples were recorded in the range of 4000-400 cm^{-1}.From IR Spectra's it was found that there was no drug-excipients interaction.

Pre compressional studies: The powder blend was subjected to pre formulation parameters like Bulk density, Tapped density,A ngle of repose,Compressibility index, Hausner's ratio.

Post-compression parameters: The tablets of different formulations were physically characterized by parameters like Thickness, Average Weight, Hardness and Friability, Uniformity of weight, In-vitro dissolution studies.

Table.1.Formulation of Terbutaline sulphate tablets with sustained release polymers

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Terbutaline sulphate	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
HPMC K 15	30	55	25	-	40	35	30	-	20	15
HPMC K4M	30	-	25	45	-	-	-	25		
Ethyl cellulose	30	35	40	45	50	55	60	65	70	75
Isopropyl Alcohol	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Lactose	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
PVP K 30	5	5	5	5	5	5	5	5	5	5
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total	**120**	**120**	**120**	**120**	**120**	**120**	**120**	**120**	**120**	**120**

Table.2.Pre-compression parameters

Powder blend	Angle of Repose (°)	bulk density (g/cc)	Tapped density (g/cc)	Compressibility index (%)	Hausner ratio
F1	22.4	0.463	0.529	18.2	1.18
F2	26.5	0.457	0.538	19.22	1.22
F3	25.66	0.466	0.505	15.58	1.22
F4	23.99	0.525	0.669	17.18	1.16
F5	24.3	0.501	0.648	18.1	1.20
F6	28.97	0.453	0.575	19.12	1.21
F7	24.84	0.432	0.55	17.17	1.19
F8	21.99	0.525	0.52	19.78	1.23
F9	29	0.501	0.669	16.61	1.24
F10	28.97	0.451	0.648	20.73	1.26

Table.4.Post-compression parameters

Formulations	Average Weight (mg)	Friability (%)	Hardness (Kg/cm^2)	Thickness (mm)
F1	120±.01	0.38±0.02	3±0.2	4.22
F2	120±0.13	0.545±0.03	3.5±0.65	4.32
F3	120±0.24	0.676±0.52	4±0.25	4.38
F4	120±0.05	0.432±0.032	4.5±0.17	4.44
F5	120±0.6	0.298±0.01	5±0.15	4.18
F6	120±0.20	0.156±0.020	4±0.62	4.1
F7	120±0.25	0.478±0.6	5±0.38	4.32
F8	120±0.28	0.436±0.32	4.5±0.35	4.32
F9	120±0.65	0.529±0.07	4±0.45	4.38
F10	120±0.71	0.683±0.030	4.5±0.30	4.44

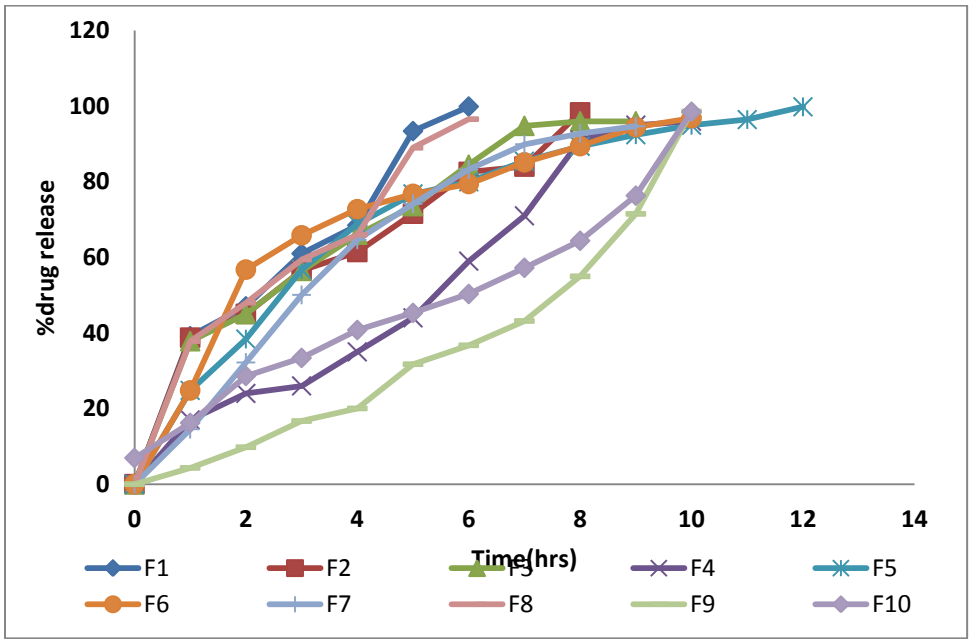

Fig.7.Cumulative %drug release of formulations F1to F10

CONCLUSION

The experimental work was carried out to prepare sustained release tablets of long acting turbutaline sulphate. Terbutalinesulphate is a class II drug according to BCS with a half life of 3-4 hours. It is administered thrice a day which results in ineffective therapy. Being half life less there is always a need for dosing frequency. Decreasing dosing frequency will increase the patient compliance for asthmatic patients and thus avoiding dosing at odd hours. Terbutaline sulphate is available in market in different immediate release dosage forms. After some time plasma concentration level decreases below MEC. So the necessity of producing the drug in sustained release formulation. So attempt is made to formulate terbutaline sulphate in sustained release formulation with different ratios of HPMC K15 polymer so that it can provide effective drug release up to 12 hours. The results of the present study showed that the polymer ratio used in the formulation F5 showed optimized result and released the drug up to 12 hours. The Terbutaline sulphate sustained release tablets containing polymer HPMC K 15 showed better release based on the drug release which showed percent drug release approximately 99 % within 8 - 12 hours.

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