ISSN: 0975-766X
CODEN: IJPTFI
Available Online through
www.ijptonline.com
Research Article

OPTIMIZATION AND EVALUATION OF TERBUTALINE SULPHATE TRANSDERMAL FILM.

Das Saumya[1]*, Pattanayak Dharmajit[1], Sahu Nigam Prasad[2]
[1]Department of Pharmaceutics, Vikas College of Pharmaceutical Sciences, Rayanigudem, Suryapet, Dist-Nalgonda, A.P-508376.
[2]Cipla Ltd. Baddi, Malpur upper, Dist-Solan, Tehesil-Nalagarh, H.P, Pin-173205.
Email: saumyaranidas@gmail.com

Received on 03-11-2011 *Accepted on 17-11-2011*

Abstract

The present investigation was aimed to formulate transdermal films incorporating Terbutaline Sulphate, a drug used in the treatment and management of Asthma. The two different polymers like ethyl cellulose (EC) and Poly Vinyl Pyrrolidone (PVP) were used in varying ratios. Polyvinyl alcohol is used as backing membrane. The polymeric films were evaluated for their physical properties like physical appearance, thickness, drug content, moisture content, folding endurance, *in-vitro* evaluation and stability studies. The FT-IR spectra analysis of physical mixture in ratio 1:1 containing drug and polymer showed no shift in peak hence no interactions. Formulation TEP5 showed satisfactory results and hence was optimised.

Key words: Terbutaline Sulphate, ethyl cellulose (EC), Poly Vinyl Pyrrolidone (PVP)

Introduction

Terbutaline Sulphate is widely used for the therapeutic management of chronic as well as prophylaxis of asthma and nocturnal asthma in particular It is a drug of choice for the treatment of asthma but it has several drawbacks such as short biological half-life of about 3.6 hours, it is readily metabolized in the gut wall and liver when given orally. It has a short duration of action, low peak plasma level of 1.2 g/ml and poor bioavailability of only 14.8%. These factors necessitated formulation of controlled release transdermal drug delivery system for terbutaline sulphate, as this route of drug administration would reduce the dosing frequency hence better patient compliance.

Materials and Method

Terbutaline sulphate was obtained as gift sample from Gitra Lab, Ahmedabad. EC and PVP were procured from S.D fine chemicals Ltd. Mumbai. All the chemicals and reagents used were of analytical reagent grade.

Preparation of backing membrane:

The backing membrane was prepared by heating 4%w/v PVA in distil water at temperature of 80^{o}C for 45min. The above solution was poured into the glass mould lined with aluminium foil to cast for a period of 6h at 60^{o}C in a hot air oven.

Preparation of Transdermal films:

The required quantity of polymers were weighed accurately as given in table no. 1 and dissolved in acetone by continuous stirring with the help of magnetic stirrer. About 40% propylene glycol and 4% tween 80 of polymer weight were added to the above solution as a plasticiser and permeation enhancer respectively. Drug was dissolved in small portion of acetone separately and added drop wise to above polymeric solution. The above solution was kept in sonicator for 15min and poured over the dried backing membrane and kept at room temprature for 24h.

Table No.1 Formulation Design and various evaluation parameters.

Sl. No	Formulation Code	Ratio of polymers (EC:PVP)	Thickness (mm)	Drug Content (%)	Moisture Content (%)	Moisture uptake	
						75% RH	85% RH
1	TEP1	1:2	0.41	91.20	9.36	3.09	11.05
2	TEP2	1:4	0.39	89.28	10.5	4.29	13.93
3	TEP3	1:6	0.40	95.80	10.73	4.24	12.43
4	TEP4	2:1	0.36	97.59	6.06	2.44	8.02
5	TEP5	4:1	0.38	98.79	8.73	2.18	7.24
6	TEP6	6:1	0.40	89.75	9.08	2.19	6.82

Evaluation of Transdermal films:

Physical Appearance:

All the Transdermal Films were visually inspected for colour clarity, flexibility and smoothness.

Thickness of the films: The thickness of the films was assessed at six different points of the films using vernier

calliper. For each formulation three randomly selected films were used.

Drug content:

1 cm^2 of the TDDS films was dissolved in 100 ml of Phosphate Buffer pH 7.4 and kept the solution for 6 h. Contents were filtered using Whatman filter paper and the filtrate was examined for the drug content against the reference solution consisting of placebo film (containing no drug) at 276 nm by using UV- spectrophotometer.

Moisture content:

The films were weighed individually and kept in a desiccator containing calcium Chloride at 37 ℃ for 24 h. The final weight was noted when there were no further changes in the weight of individual films. The percentage of moisture content was calculated as a difference between initial and final weight with respect to final weight.

Moisture uptake:

Weighed films kept in a desiccator at 40 °C for 24 h was taken out and exposed to relative humidity of 75 % (Saturated solution of NaCl) and 85 % (Standard solution of potassium chloride) respectively at room temperature. Then the films were measured periodically to constant weight.

Weight variation:

Five different films from individual batches were weighed individually and the average weight was calculated. The individual should not deviate significantly from the average weight. That test was performed on films which were dried at 60°C for 4 h prior to testing.

Folding endurance:

Folding endurance of the film was determined manually by folding a small strip of the film at the same place till it breaks. The maximum number folding operations done at the same place of the film without breaking gives the value of folding endurance. The cracking point of the film was considered as the end point.

In vitro permeation study: Franz diffusion cell using Dialysis Membrane:

The transdermal system of 2.83 cm^2 area was placed in intimate contact with dialysis membrane and was fixed to donor compartment, which is filled with 44 ml of phosphate buffer 7.4 pH as diffusion medium in diffusion cell. The amount of drug released was determined by withdrawing 1 ml of sample and diluting it to 10 ml at specific time intervals for 24 h. The volume withdrawn is replaced with an equal volume of fresh, pre warmed (37^0C)

phosphate buffer pH 7.4.

Stability studies:

The effect of ageing on physical appearance was studied by packing the polymeric films in properly sealed aluminium foils and then stored in desiccator at ambient conditions for 30 d.

Results

All the films were having good physical appearance. The thickness of all films was found to be uniform and it ranges from 0.36 mm to 0.41 mm. Thus the films passed physical examination. The drug content of all formulations was found to be satisfactory. The moisture content of all the formulations ranged from 6.06 % to 10.73 %. The moisture uptake of all the formulations ranged from 2.18 % to 9.98 % in 75 % RH and 6.32 % to 13.93 % in 84 % RH. Moisture uptake and moisture content of transdermal formulations were in range because of the hydrophobic nature of the polymers. Weight variation of all the transdermal formulations was in the ranges of 16.60±0.60 to 29.87±0.27. Folding endurance was found to be varied between 74 to 112 numbers of times. The *in vitro* drug release profile of prepared transdermal formulations exhibited a sustained pattern, in controlled manner over extended period of time. The release pattern of all the formulations was represented in Fig.1. From the drug release data, the transdermal formulation TEP5 was found to release the drug up to 87.375 % at 24 h, thus concluded to have sustained release of drug in constant manner for longer period of time when compared to other transdermal formulation. The stability studies were performed for the period of 60 d at room temperature at 40 % RH and the satisfactory results were obtained with providing a safety profile of storage of Terbutaline Sulphate transdermal films.

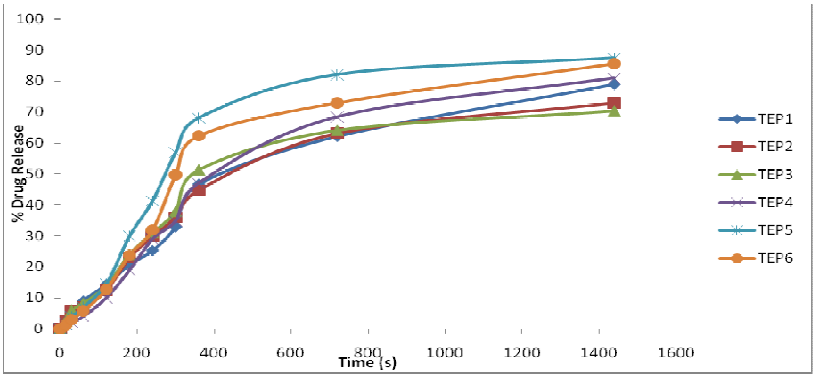

Fig. No.1 Comparison of in-vitro permeation rate profile of Terbutaline sulphate Transdermal Film.

Discussion

The physicochemical parameters like thickness, drug content, moisture uptake, weight variation and folding endurance showed good results for all formulations. Formulations TEP1 to TEP6 showed less fluctuation. Among the release profile TEP5 which contains EC:PVP in ratio 4:1 showed the consistent release without fluctuation. Hence it is concluded that TDDS formulated using EC and PVP in optimum ratios can enhance drug release for a prolong period of time.

References

1. Y. W. Chien, Concepts and system design for the rate controlled drug delivery systems, in: Novel drug delivery systems, 2nd edn, Drug and Pharmaceutical Sciences, Marcel Dekker Inc., New York, 1992; 50: pp. 1-139and 529-540.
2. G. W. Cleary. Transdermal and transdermal-like delivery system opportunities: Today and the future. Drug Del. Tech. 2003; 3:1-2.
3. J. R. Robinson and H. L Vincent, Controlled drug delivery fundamentals and applications. 2nd edn, Revised and Expanded: Lee. Marcel Dekker Inc; 2005: pp. 524-525.
4. U. Pison, T. Wette, M. Giersig and A. David, Nanomedicine for respiratory diseases, Eur J Pharmacol 2006, 533: 341-350.
5. R. Mehta, Topical and transdermal drug delivery: What a Pharmacist Needs to Know, ACEP; 1-10.
6. Y. W. Chein, Transdermal Drug Delivery Systems and Delivery Systems. 2nd edn, Marcel Dekker Inc., New York 1992: pp. 301-315
7. P. C. Wu, Y. B. Huang, Judy Jui-Fen Chang, Jui-Sheng Chang and Yi-Hung Tsai, Evaluation of pharmacokinetics and pharmacodynamics of captopril from transdermal hydrophilic gels in normotensive rabbits and spontaneously hypertensive rats, Int J Pharm 2000; 209: 87-94.
8. D. C. G. Murthy, S. Y. David. Pharmaceutical product development *in vitro – in vivo*, correlation. 1st edn, Informa Healthcare, USA Inc; 2007: pp. 153-154.
9. Libermann and Lachman, Pharmaceutical dosage forms, 2nd edn, Lea and Febiger; 1990: pp. 265-271
10. A. M Wokovich, S. Prodduturi, W. H Doub, A. S. Hussain and L.F. Buhse, Transdermal drug delivery

system (TDDS) adhesion as a critical safety, efficacy and quality attribute, Eur J Pharm and Biopharm 2006; 64: 1–8.

11. H. Ansel, L. Allen and N. Popovich, Pharmaceutical dosage form and drug delivery system, 7th edn, (International student edition): Lippincot Williams & Wilkins Publishers; 2000: pp. 249-250.
12. Y. N Kalia and R. H Guy. Modeling transdermal drug release. Adv Drug Del Rev 2001; 48: 159–72.
13. R. J. Babu and J. K. Pandit , Effect of penetration enhancers on the release and skin permeation of bupranolol from reservoir-type transdermal delivery systems, Int J Pharm 2005; 288: 325–334.
14. M. K. Kim, H. Zhao, C. H. Lee and D. D. Kim, Formulation of a reservoir-type testosterone transdermal delivery system, Int J Pharm 2001; 219: 51–59
15. L. Panigrahi, S. K. Ghosal, S. Pattnaik, L. Maharana and B. B. Barik, Effect of permeation enhancer on the release and permeation kinetics of lincomycin hydrochloride gel formulation through mouse skin, Ind J Pharm Sci 2006; 68 (2): 205-211.
16. B. Mukherjee, Kanupriya, S. Mahapatra, S. Das and B. Patra, Sorbitan monolaurate-20 as a potential skin permeation enhancer in transdermal patches, The J Appl Res 2005; 5 (1): 96-101.
17. A. mehdizadeh, T. Toliate, M. R. Rouini, S. Abashzadeh and D. Farid, Design and *in vitro* evaluation of new drug-in-adhesive formulations of fentanyl transdermal patches, Acta Pharm 2004; 54: 301–17.
18. P. F. C. Lim, X. Y. Liu , L. Kang, C. L. H Paul, Y. W. Chanc and S. Y. Chan, Limonene GP1/PG organogel as a vehicle in transdermal delivery of haloperidol, Int J Pharm 2006; 311:157–164.
19. P. M. Dandagi, F. V. Manvi, A. P. Gadad, V. S. Mastiholimath and T. Jagadeesh, Formulation of a Transdermal drug delivery system of ketotifen fumarate, Ind J Pharm Sci 2003; 65 (3): 239-43.

Corresponding Author:

Das Saumya*

Department of Pharmaceutics,

Vikas College of Pharmaceutical Sciences,

Rayanigudem, Suryapet, Dist- Nalgonda, A.P-508376.

Email: *saumyaranidas@gmail.com*