Research Article

Formulation and Evaluation of Transdermal Patch of Blonanserin

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ABSTRACT

The objective of the present study was to formulate and evaluate transdermal patch of Blonanserin. Blonanserin transdermal patches were prepared by solvent casting method using natural and synthetic polymer. Various plastisizer were screened along with polymers. Drug excipient compatibility studies concluded that the drug and excipient are compatible with each other. The prepared patches were evaluated for physico-chemical parameters to justify their suitability for transdermal use. Formulations containing Xanthan Gum with plasticizer propylene glycol gives best drug release in 8 hours. More than 90% drug release found after 8 hours in formulation F5. Hence F5 formulation is considered as optimized batch. F5 batch was found stable during stability study. Blonanserin transdermal patches were successfully prepared by solvent casting method using Xanthan Gum natural polymer.

Keywords: Blonanserin, Transdermal Patch, formulation, TDDS.

INTRODUCTION

During the past few years, interest in the development of novel drug delivery systems for existing drug molecules has been renewed. The development of a novel delivery system for existing drug molecules not only improves the drug's performance in terms of efficacy and safety but also improves patient compliance and overall therapeutic benefit to a significant extent. [1] Transdermal Drug Delivery System (TDDS) are defined as self-contained, discrete dosage forms which are also known as "patches". When patches are applied to the intact skin, deliver the drug through the skin at a controlled rate to the systemic circulation. TDDS are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin.[1] The main objective of transdermal drug delivery system is to deliver drugs into systemic circulation into the skin through skin at predetermined rate with minimal inter and intra patient variation. Currently transdermal delivery is one of the most promising methods for drug application. It reduces the load that the oral route commonly places on the digestive tract and liver. It enhances patient compliances and minimizes harmful side effects of a drug caused from temporary over dose and is convenience in transdermal delivered drugs that require only once weakly application.[2] That wills improves bioavailability, more uniform plasma levels, longer duration of action resulting in a reduction in dosing frequency, reduced side effects and improved therapy due to maintenance of plasma levels up to the end of the dosing interval compared to a decline in plasma levels with conventional oral dosage forms. Transdermal delivery not only provides controlled, constant administration of drugs, but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into systemic circulation, which often causes undesirable side effects.[2] Several important advantages of transdermal drug delivery are limitations of hepatic first pass metabolism, enhancement of therapeutic efficacy and maintenance of steady plasma level of drug. The developments of TDDS is a multidisciplinary activity that encompasses fundamental feasibility studies starting from the selection of drug molecule to the demonstration of sufficient drug flux in an *ex vivo* and *in vivo* model followed by fabrication of a drug delivery system that meets all the stringent needs that are specific to the drug molecule (physicochemical, stability factors), the patient (comfort and cosmetic appeal), the manufacturer (scale up and manufacturability) and most important economy.[2] The first transdermal system, Transdermal SCOP was approved by FDA in 1979 for the prevention of nausea and vomiting associated with travel. Most transdermal patches are designed to release the active ingredient at a zero order rate for a period of several hours to days following application to the skin. This is especially advantageous for prophylactic therapy in chronic conditions. The evidence of percutaneous drug absorption may be found through measurable blood levels of the drug, detectable excretion of the drug and its metabolites in the urine and through the clinical response of the patient to the administered drug therapy.[2]

Transdermal route and drug delivery prospects[3]

Skin

The largest organ

The skin is the largest organ of the human body which covers a surface area of approximately 2 sq. m. and receives about one third of the blood circulation through the body. It serves as a permeability barrier against the transdermal absorption of various chemical and biological agents. It is one of the most readily available organs of the body with a thickness of few millimeters which,

→ Separates the underlying blood circulation network from the outside environment

→ Serves as a barrier against physical, chemical and microbiological attacks.

→ Acts as a thermostat in maintaining body temperature.

→ Plays role in the regulation of blood pressure.

→ Protects against the penetration of UV rays.

→ Skin is a major factor in determining the various drug delivery aspects like permeation and absorption of drug across the dermis. The diffusional resistance of the skin is greatly dependent on its anatomy and ultra-structure.

MATERIALS

Blonanserin was given as a gift sample from Torrent Research Centre, Ahmedabad, Sodium CMC Xanthan Gum Chitosan, Triethyl Citrate PEG 400 Propylene Glycol and Glycerin from Balaji Chemicals, Ahmedabad used as a material for the transdermal patch

METHODS

Pre-formulation Study of Drug

Characterization of Drug

By checking its visual appearance, odour and solubility in various solvents like Water, 6.8 phosphate buffer and ethanol.

Preparation of Sample solution

From the stock solution further dilutions were done with the respective solvents and prepared solutions in the concentration range of 5-30 µg with 7.4 phosphate buffer.

Dose Calculation of Blonanserin for Transdermal Patch

- Transdermal Dose = (Oral dose X Bioavailability)/100

- Transdermal Dose = (2 X 55)/100

- Transdermal Dose = 1.1 mg Blonanserin

- Diameter of the Petridish = 9 cm

- Radius = Diameter/2 = 9/2 = 4.5 cm.

- Area of Petridish A= πr^2 =3.14 X 4.5 X 4.5 = 63.58 cm2

- Now, Dose is 1.1 mg and cut the pieces in 2 cm X 2 cm = 4 cm2

- 4 cm2 contain 1.1 mg drug,

- So, 63.58 cm2 contain (?)

- Amount of Drug ~ 17.5 mg each batch.

Preparation of transdermal patches

All the ingredients were weighed accurately and dissolved in a suitable solvent with continuous stirring. Then plasticizer was added to the above solution. The resultant solution was stirred for 15 min to get a clear solution and was kept aside for some time to get a bubble free solution, these solutions were casted slowly on a petri plate with a continuous flow to avoid bubble formation and the plates were kept at room temperature for 24 hrs. An inverted funnel was placed over the plate to control the rate of drying. After 24 hr, formed patch was taken out and checked for its complete dryness. The dried patch was gently separated from the petri plate and cut into separate patches 2 x 2 cm area. The patches were preserved by wrapping in aluminum foil. These patches were used for evaluation tests further

Evaluation of Transdermal Patches

Appearance

Check the visual appearance of the prepared Transdermal patches and record the same.

Thickness

The thickness of the prepared patches was measured using digital vernier caliper with a least count of 0.01 mm at different spots of the patch. The thickness was measured at three different spots of the patches and average was taken and SD was calculated.

Weight Variation

Four-centimeter square of the patch was cut at three different places from the casted film. The weight of each film was taken and weight variation was calculated.

Folding Endurance

Folding endurance was determined by repeated folding of the patch at the same place till the strip breaks. The number of times the patch is folded without breaking was computed as the folding endurance value.

Surface pH

The surface pH of prepared transdermal patch was determined using pH meter. Patch was slightly wet with the help of water. The pH was measured by bringing the electrode in contact with the surface of the patch. The procedure was performed in triplicate and average with standard deviation was reported.

Drug Content

Drug content test of the patch was carried out by dissolving the 4 cm²patch in 100 ml of pH 7.4 phosphate buffer. The

prepared solution was filtered and then measured spectrophotometrically at λ_{max} of 237 nm. The determination was carried out in triplicate for all the formulations and average with standard deviation was recorded.

Percentage Elongation

The percentage elongation was determined by noting the length just before the break point and calculating the same by using below mentioned equation.

Percentage Elongation = (L1-L2/L1) x 100

Where, L1is the final length of each patch andL2 is the initial length of each patch

In Vitro Diffusion Study

In Vitro Drug Diffusion studies was carried out using the 20 ml Franz diffusion cell. The synthetic membrane was used as a skin. The membrane was stabilized before mounting to remove the soluble components. The membrane was mounted between the donor and receptor compartments. The receptor compartment was filled with 20 ml of isotonic phosphate buffer of pH 7.4 which was maintained at 37± 0.2°C and hydrodynamics were maintained using magnetic stirrer. One patch of dimension 2 cm × 2 cm was previously moistened with a few drops of pH 7.4 phosphate buffer and placed in donor compartment. 1 ml samples from receptor compartment were withdrawn at suitable time interval of 1, 2, 3, 4, 6 and 8 hours which was then replaced with 1 ml of pH 7.4 phosphate buffer. The percentage of drug permeated was determined by measuring the absorbance in UV Visible spectrophotometer at λ_{max} of 237 nm.

Stability study

Stability study was carried out at 40°C/75% RH condition for 1 month. Each piece of the patch from the optimized formulation was packed in butter paper followed by aluminum foil. After 1 month, the patches were evaluated for the physical appearance, drug content and diffusion study.

RESULTS AND DISCUSSION

Evaluation of Transdermal patches of Blonanserin

Transdermal patches of Blonanserin have been initiated to achieve the targeted objectives. The product development was initiated with the selection of polymers for patch formation. Total three type of polymers and three different type of plastIsizer was selected and trials taken. The evaluation parameters were checked and recorded as below;

Table 1: Evaluation parameters of Blonanserin Transdermal Patches

Batch	Surface	Transparency	Stickiness
F1	Smooth	Transparent	Non-Sticky
F2	Smooth	Transparent	Non-Sticky
F3	Smooth	Transparent	Non-Sticky
F4	Smooth	Transparent	Non-Sticky
F5	Smooth	Transparent	Non-Sticky
F6	Smooth	Transparent	Non-Sticky
F7	Smooth	Transparent	Non-Sticky
F8	Smooth	Transparent	Non-Sticky
F9	Smooth	Transparent	Non-Sticky
F10	Smooth	Transparent	Non-Sticky
F11	Smooth	Transparent	Non-Sticky
F12	Smooth	Transparent	Non-Sticky
F13	Smooth	Transparent	Non-Sticky
F14	Smooth	Transparent	Non-Sticky
F15	Smooth	Transparent	Non-Sticky

Based on the appearance results, it was observed that all nine batches were found non-sticky in nature. The patches were transparent and smooth in surface. It was concluded that all excipients were found in solubilize form and no any un-dissolve particles are present in the preparation.

Table 2: Evaluation parameters of Blonanserin Transdermal Patches

Batch	Weight variation (mg)± SD	Thickness (mm) ± SD	Surface pH± SD
F1	105 ± 3.1	0.26 ± 0.04	7.0 ± 0.2
F2	101 ± 4.7	0.25 ± 0.02	6.8 ± 0.4
F3	107 ± 4.1	0.25 ± 0.05	7.1 ± 0.3
F4	105 ± 3.6	0.23 ± 0.06	7.0 ± 0.3
F5	104 ± 2.8	0.24 ± 0.04	6.9 ± 0.2
F6	101 ± 3.2	0.23 ± 0.05	7.0 ± 0.2
F7	105 ± 2.0	0.25 ± 0.04	6.9 ± 0.3
F8	102 ± 3.3	0.26 ± 0.03	7.0 ± 0.2
F9	107 ± 2.8	0.22 ± 0.05	6.9 ± 0.1
F10	108 ± 2.1	0.21 ± 0.04	6.7 ± 0.3
F11	101 ± 1.9	0.20 ± 0.02	6.8 ± 0.4
F12	105 ± 2.6	0.22 ± 0.01	6.9 ± 0.2
F13	107 ± 1.7	0.21 ± 0.04	6.7 ± 0.4
F14	104 ± 2.2	0.22 ± 0.03	6.8 ± 0.3
F15	106 ± 3.1	0.22 ± 0.04	6.7 ± 0.2

Based on the above weight variation, thickness and surface pH results, it was observed that the all F1-F15 batches were found satisfactory in terms of weight variation test. The weight variation was found well within acceptable range. The thickness of patches was found uniform in nature and the variation is found satisfactory. Further, the surface pH of the patches was found between 6.8 to 7.1 and it is acceptable.

Table 3: Evaluation of Blonanserin Transdermal Patches

Batch	Drug Content (%)± SD	Folding Endurance ± SD	% Elongation
F1	97.5 ± 3.5	125 ± 8	3.5 ± 1.6
F2	98.3 ± 3.9	172 ± 5	3.7 ± 1.3
F3	98.2 ± 3.1	191 ± 9	4.1 ± 1.5
F4	98.9 ± 3.7	302 ± 7	2.6 ± 1.4
F5	98.7 ± 3.4	314 ± 3	2.8 ± 1.2
F6	97.6 ± 3.8	330 ± 8	2.9 ± 1.5
F7	98.5 ± 3.3	158 ± 5	3.3 ± 1.3
F8	99.1 ± 3.5	172 ± 7	4.1 ± 1.7
F9	99.0 ± 3.7	191 ± 8	4.8 ± 1.4
F10	98.5 ± 3.1	139 ± 7	3.9 ± 1.1
F11	98.4 ± 3.9	147 ± 5	4.1 ± 1.5
F12	98.9 ± 3.3	153 ± 9	3.8 ± 1.9
F13	98.6 ± 2.8	187 ± 4	4.0 ± 1.3
F14	99.5 ± 2.3	193 ± 6	3.5 ± 1.1
F15	99.3 ± 2.5	199 ± 8	3.1 ± 1.4

The drug content results of F1-F15 batches were recorded in above table. It was observed that the all batches were found well within acceptable limit for drug content. Most of the results are between 97% to 99.1%. It means that the drug is properly distributed into the patches. The % elongation of all batches was recorded in the above table. Based on % elongation results, it was noted that the elasticity of the film was increased with the increase in amount of polymer. Also the plastsizer amount is affecting the elongation results as it's directly proposal to elasticity of the patch.

Folding endurance results of F1 to F15 batches were found satisfactory. All polymers are giving more than 100 value of folding endurance which is sufficient for patch formulation.

Table 4: Evaluation of Drug release profile Blonanserin Transdermal Patches

% Cumulative drug release								
Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	8.5	12.5	15.2	16.2	18.1	19.5	22.8	21.6	20.1
2	16.5	18.3	20.3	29.1	31.3	36.1	39.9	37.3	36.9
3	24.5	26.3	28.1	38.9	41.5	50.5	52.4	51.7	49.1
4	31.6	33.6	35.9	51.4	54.3	59.5	61.0	58.1	56.5
5	42.3	45.8	50.1	62.5	65.8	71.3	74.7	73.3	69.5
6	53.1	56.7	59.1	73.9	76.1	80.7	79.1	76.5	75.6
7	62.9	65.3	67.3	85.7	87.3	91.4	88.9	85.7	81.7
8	71.3	76.1	78.1	96.5	99.1	97.9	95.7	94.9	92.1

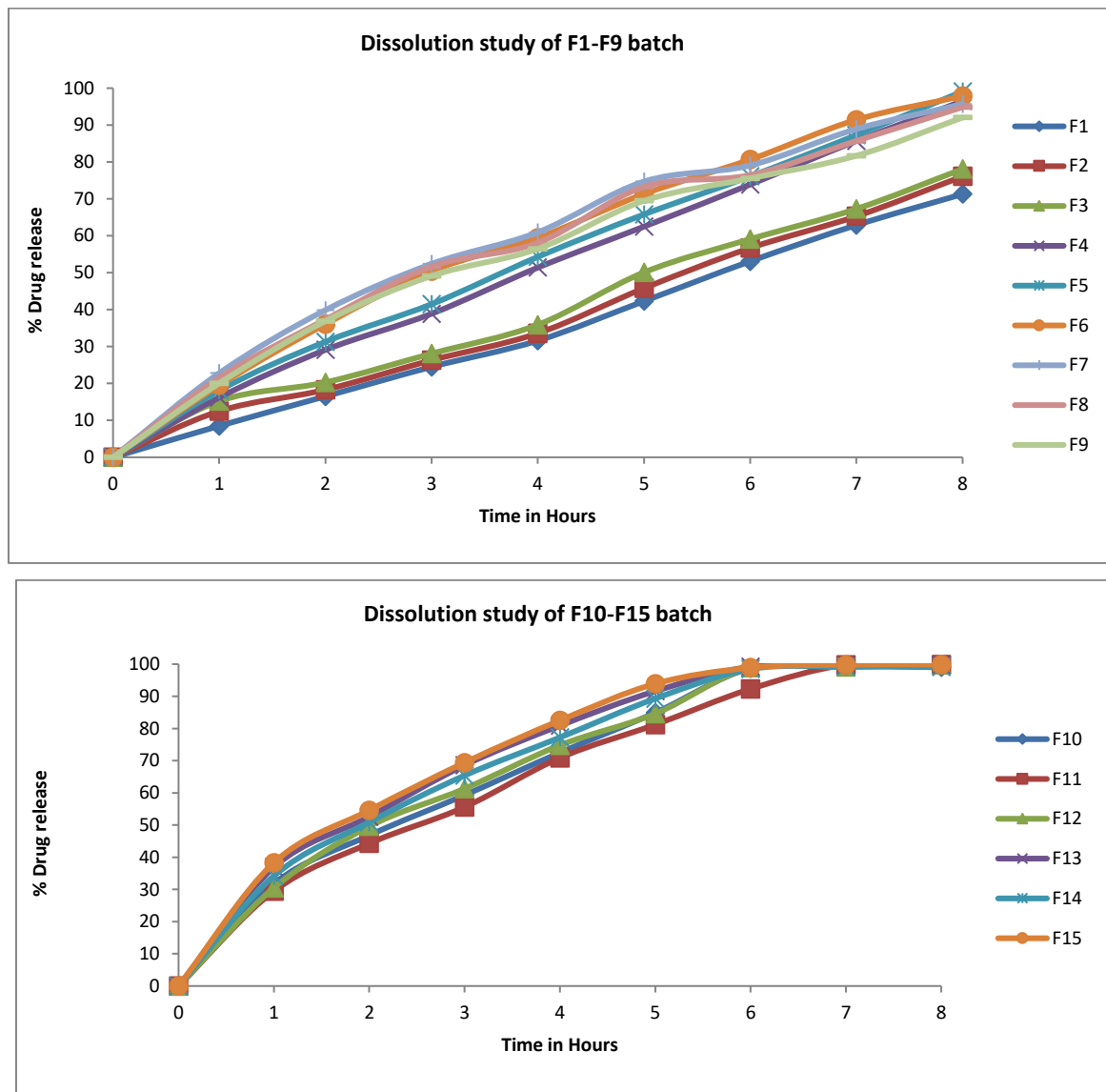| Time (hrs)	F10	F11	F12	F13	F14	F15
1	31.8	29.5	30.5	36.9	34.2	38.3
2	46.8	44.3	49.6	52.6	50.9	54.6
3	59.3	55.6	61.3	68.6	65.4	69.4
4	72.5	70.9	74.8	80.9	77.2	82.5
5	84.9	81.2	84.6	91.6	89.3	93.9
6	98.7	92.3	98.9	99.2	98.5	98.9
7	99.5	99.8	99.1	99.5	99.2	99.8
8	99.0	99.9	99.9	99.7	99.1	99.9

Figure 1: Dissolution study of Blonanserin Transdermal Patches

Based on the drug release data, it was observed that the F5 batch was the most satisfactory batch with respect to drug release and other parameters. Hence, the F5 batch selected as optimized batch and Stability study of the same batch initiated.

Stability Study

Stability study of optimized batch F5 performed for 1 month at 40°C and 75% RH. Initial results and after 1-month results compared and found satisfactory. The batch was found stable during stability. The results were recorded in below table.

Table 5: Stability study results

Parameter	Initial	After 1 Month
Appearance	Complies	Complies
Assay (%) (n=3)	99.0 ± 3.7	98.9 ± 2.5
% Drug release after 8 hours(n=3)	99.1± 1.6	98.7± 1.8

CONCLUSION

Blonanserin transdermal patches were successfully prepared by solvent casting method using different natural and synthetic polymers. Drug excipient compatibility studies concluded that the drug and excipient are compatible with each other. The prepared patches were evaluated for physico-chemical parameters to justify their suitability for transdermal use. Formulations containing Xanthan Gum with plasticizer propylene glycol gives best drug release in 8 hours. More than 90% drug release found after 8 hours in formulation F5. Hence F5 formulation is considered as optimized batch. F5 batch was found stable during stability study.

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