Available online at www.elixirpublishers.com (Elixir International Journal)

Pharmacy

Elixir Pharmacy 78 (2015) 29787-29789

ISSN: 2229-712X

Formulation development of salicylic acid derma sticks for external applications

Purushotham Rao[1], Kaushik Valambhia[2], Prabhakar Reddy[1], Ravindranath[3], Venkateshwarlu[3] and Prashant Sagare[4]

[1]H.K.E College of Pharmacy, (MR Medical College Campus), Gulbarga, K.S. India

[2]United Republic of Tanzania, Tanzania

[3]Osmania University, Hyderabad, A.P. India

[4]MR Medical College and General Hospital, Gulbarga-K.S.

ARTICLE INFO

Article history:

Received: 22 June 2011;

Received in revised form:

28 December 2014;

Accepted: 15 January 2015;

Keywords

Salicylic acid,

Medicated derma sticks.

ABSTRACT

The preparations available in the market for the treatment diseases have several disadvantages like greasiness, inconvenient to store and requires applicator or use of fingertip, which may lead to contamination. Therefore, it was found essential to find an alternative to counter all the above disadvantages effectively and hence in the present work, formulation and development of medicated derma sticks has been planned with the drug, salicylic acid that has keratolytic activity. The preparation and characterization of medicated sticks was carried out in four phases. Phase I studies includes optimization of non medicated sticks using the ointment bases with varied concentrations of waxes which is done by measuring the parameters like weight, thickness and length. From these parameters optimized formula is screened out. Phase II studies involves incorporation of medicament in the optimized formula by heating and congealing process. Phase III studies includes characterization of prepared medicated sticks for weight variation, thickness, length, size, shape and drug content uniformity. Phase IV studies involves *in vitro* drug diffusion studies by using prehydrated cellophane membrane for 160 minutes in pH 7.4 phosphate buffer showed an excellent drug release. Primary skin irritation studies carried out on guinea pigs, showed no sensitization and edema on skin after 72 hrs of application. Stability studies conducted for a period of 3 weeks and FT-IR Spectral analysis conducted. The results of present study revealed that the prepared medicated sticks of salicylic acid are convenient, equally effective, without any contamination chances on application and free from skin irritation.

Introduction

Patients express difficulty in application of ointments, creams, gels etc. results in non- compliance and ineffective therapy. Recent advance in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for application and to achieve better patient compliance. One such approach is medicated sticks[1-2]. An advantage of this drug delivery system includes patient compliance; convenience and comfort ness for efficient treatment include application without fingertip, immediate onset of action, reduced dosage regimen and economy. Salicylic acid[3-5] that has keratolytic activity, which belongs to hydroxybenzoic acid group was selected as drug candidate, as it is not available in such dosage form and widely used in treatment of warts[6-7]. Objective of the present work was to develop such a NDDS for Salicylic acid by heating and congealing method in the treatment of warts.

Materials and Methods

Salicylic acid was gift sample from S.D. fine chemicals Ltd., Mumbai. Stearyl alcohol pure, white petrolatum (Loba chemie Pvt. Ltd., Mumbai), Sodium lauryl sulphate, Cetyl Alcohol (S.D. fine chemicals ltd. Mumbai), Propylene glycol (Ranbaxy lab. Ltd., SAS Nagar), Methanol (Qualigens Fine Chemicals, Mumbai) were used.

Preparation of salicylic acid stick:

Medicated derma sticks of salicylic acid were prepared by heating and congealing according to the formulae given in Table 1.Depending upon the weight, thickenss and length of non-medicated derma sticks, the formulae is chosen for the incorporation of the drug. Stearyl alcohol[8] / Cetyl alcohol[9] and white petroleum was melted in a china dish and heated this mixutre upto 70^0C. Dissolve sodium lauryl sulfate, propylene glycol in purified water and heat the solution to 70^0C separately. Add the oleaginous phase slowly to the aqueous phase, stirring constantly and then the drug was added slowly with continuous stirring in order to get a uniform mixture in optimized formulation. The hot mixture was poured into the glass mould and cooled to get the desired shape of sticks. The stick was removed from the mould after 24 hours with the help of plunger and inserted into the medicated derma stick container.

Evaluation of sticks:

Three sticks were selected randomly and weighed individually. The individual weights were compared with the average weight for determination of weight variation. As the shape of the stick is cylindrical the thickness and length was determined with the help of screw gauge and vernier calliper respectively. The average thickness was measured, by observing thickness at three different parts of the stick. For drug content

Tele:

E-mail addresses: kprao369@rediffmail.com

uniformity the stick equivalent to 50 mg of salicylic acid was extracted with methanol and liquid was filtered. The salicylic acid content was determined by measuring the absorbance at 231 after appropriate dilution with methanol. The drug content was calculated using the standard calibration curve. The mean percent was calculated as an average of three determinations. IR spectra of salicylic acid and its excipients of the formulations were obtained by KBr pellet method using Perkin – Elmer FTIR series (model – 1615) spectrophotometer in order to rule out drug carrier interactions.

***In vitro* drug diffusion studies:**[10]

In vitro drug diffusion salicylic acid sticks was studied using permeation cell which is made up of a glass cylinder with both ends open, 10 cm height, 3.7 cm outer diameter and 3.1cm. inner diameter. A cellophane membrane soaked in distilled water (24 hrs. before use) was fixed to the one end of the cylinder. Stick containing one gram of salicylic acid was taken in the cell (donor compartment) and rubbed, then the cell was immersed in beaker containing 100 ml of drug free pH 7.5 phosphate buffer[11] (receptor compartment). The cell was immersed to a depth of 1 cm. below the surface of the receptor fluid. The medium in the receptor compartment was agitated using a magnetic stirrer and a temperature of 37^{o}C ± 1°C was maintained. Samples (5 ml) of the receptor compartment were withdrawn at specified intervals over a period of 160 min and analyzed for drug content by measuring the absorbance at 231 nm. The volume of sample withdrawn at each interval was replaced with a fresh quantity of diffusion medium. Cumulative percent of salicylic acid released was calculated and plotted against time.

Primary skin irritation test:

This test is conducted on 3 healthy guinea pigs (2 male and 1 female), which were supplied with fresh food and water during the test period. 24 hours prior to test, the hair from the lower abdominal portion was shaved to expose sufficiently large test area. The test site was cleaned with surgical spirit then medicated stick is applied to test area. The test site was observed for erythema and edema for 24, 48 and 72 hrs. after application. This test was conducted to evaluate the irritancy of the prepared medicated stick on the intact skin of guinea pig.

Stability Studies:

Short-term stability studies on the promising formulation MS1 were carried out by storing the sticks at 27±2°C for a period of three weeks. At intervals of one week the sticks were visually examined for drug content uniformity and any physical change.

Results and Discussion

Medicated sticks of salicylic acid were prepared by heating and congealing method using Stearyl alcohol as stiffening agent while petrolatum used as emollient, propylene glycol and sodium lauryl sulphate were used as humectants and emulsifying agent respectively. A total of six formulations were designed.As the material was uniformly filled in mould with uniform length and diameter, the sticks obtained were of uniform length, thickness and weight respectively. The drug content was found to be 95.26 to 99.40 % as shown in Table 2. Among the formulations, various concentrations of Stearyl alcohol (13.8 to 23% w/w) was employed as stiffening agent. The in vitro drug diffusion was carried out for all the formulations i.e. MS1, MS2, MS3, MS4, MS5 and MS6 in pH 7.5-phosphate buffer over a period of 160 minutes (Table 3).. The data reveals that overall, formulation MS1 showed the maximum 69.15% of drug release in 160 minutes as compared to other forrmulations. IR spectroscopic studies indicate that the drug is compatible with all the excipients. The IR spectra of MS1 showed all the characteristic peaks of Salicylic acid pure drug, thus confirming that no interaction of drug observed with the component of the formulations.

References

1. Fuchs P, Schopflin G. Medicated sticks, United States patent 3,856, 931: Berlin: 1974.
2. Fuchs P, Schopflin G. Medicated sticks, United States patent 3,211, 618, 931: Berlin: 1974.
3. Indian pharmacopoeia, Vol. II, 4th ed. New Delhi: The control of publications; 1996. p. 673.
4. British pharmacopoeia, Vol. II, Her Majesty's Stationary Office for the Department of Health; 3rd ed., London; 2008. p. 1920-22.
5. United States Pharmacopoeia, Vol. III, Port city press: Asian ed. US; 2007. p.3154-55.
6. Kumar V, Cotran RS, Robbin SL. Basic pathology, 6th ed. Harcourt India pvt. Ltd: New Delhi; 2001. p. 705-7.
7. Berkow R. editor. The merck manual, 14th ed. Merck Sharp and Dohme: Merck Co. Inc; 1982. p. 2046.
8. Aniley W, Paul WJ. Hand book of pharamaceutical excipients: profile of stearyl alcohol. The pharamaceutical Press: London; 1994. p. 498.
9. Aniley W, Paul WJ. Hand book of pharamaceutical excipients: profile of cetyl alcohol. The pharamaceutical Press: London; 1994. p. 99.
10. Indian pharmacopoeia, Vol. II, 4th ed. New Delhi: The control of publications; 1996. p. A-147.
11. Bango R, Jayakar B. Diffusion studies on salicylic acid ointment through rabbit skin. The Indian Journal of Hospital Pharmacy; 1997; 51- 2.

Table 1: composition of different batches of salicylic acid sticks

Ingredients (mg/stick)	Formulation code		
	MS1	MS2	MS3
Salicylic acid	8	8	8
Stearyl alcohol	13.8	18.4	23
White petrolatum	32.2	27.6	23
Sodium lauryl sulphate	0.92	0.92	0.92
Propylene glycol	11.04	11.04	11.04
Purified water	34.04	34.04	34.04

Table 2: Evaluation of Medicated Sticks

Formulation code	Medicated stick			Drug content (%) Salicylic acid*
	Weight* (gm)	Thickness* (mm)	Length* (cm	
	Mean ± SD	Mean ± SD	Mean ± SD	
MS – 1	1.59 ± 0.02	6.64 ± 0.02	4 ± 0.01	99.40
MS – 2	1.60 ± 0.02	6.40 ± 0.03	4 ± 0.02	96.25
MS – 3	1.60 ± 0.01	6.38 ± 0.04	4 ± 0.02	95.26

* Each reading is an average of three determinations

Table 3: *Invitro* Drug Release Of Salicylic Acid Sticks in Ph 7.5 Phosphate Buffer

Sl. No	Time (min)	%Cumulative Drug released*		
		MS 1	MS 2	MS 3
1	00	0.00 ± 0.00	0.00 ±0.00	0.00 ± 0.00
2	20	2.61 ± 0.13	5.66 ± 0.16	10.5 ± 0.25
3.	40	18.61 ±0.17	15.60 ± 0.34	16.74 ± 0.16
4.	60	22.64 ±0.25	20.80 ± 0.58	23.99 ± 0.38
5.	80	29.89 ±0.36	23.75 ± 0.45	31.62 ± 0.45
6.	100	41.56 ±0.47	27.70 ± 0.68	35.15 ± 0.68
7.	120	46.62 ±0.68	31.81 ± 0.23	38.23 ± 0.78
8.	140	57.97 ±0.72	35.16 ± 0.79	40.97 ± 0.52
9.	160	69.15 ±0.91	36.11 ± 0.64	50.61 ± 0.41

* Each reading is an average of three determinations
* One gm of sample contains 80 mg of drug