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Research: Formulation and Evaluation of an Anti-Acne Dermal Sticks

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ABSTRACT: The recent work, formulation and development of medicated Anti-acne dermal sticks has been planned with the drug, Dapsone that has anti-acne activity. The preparation and characterization of medicated sticks were carried out in different phases. Phase I studies include preparation and evaluation of medicated derma sticks using the ointment bases with varied concentrations of waxes and incorporation of medicament in the optimized formula by heating and congealing process. The formulation of medicated sticks was carried out which includes preparation of medicated derma sticks Then evaluation of prepared medicated sticks for weight variation, thickness, length, size and shape, physical appearance, softening point, breaking point, drug content uniformity, in vitro drug diffusion studies by using pre-hydrated cellophane membrane by using Franz diffusion cell for 480 minutes in pH 7.4 phosphate buffer and Stability studies Objective of the present work was to develop a TDDS of Dapsone prepared by heating and congealing method a convenient model to use by patients. [1]

INTRODUCTION: In the past few decades, significant medical advances have been made in the area of drug delivery. The area of medicated sticks as a delivery system has developed at a faster rate as topical drug delivery systems.[2] Many topical analgesic formulations such as ointments, creams, forms, gels etc. are available in market, but some patients express difficulty in application which results in non- compliance and ineffective therapy. Recent advances 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, immediate onset of action, reduced dosage regimen and economy, One such approach is medicated sticks. Skin break out Vulgari is a repetitively scatter influencing all persons at any rate once during life. The term skin breaks out from the Greek word 'summit' from the works of Actius Amadeus. He utilized this term "top" in the feeling of skin emission" and Vulgaris demonstrate the signifying "basic dermatologic wellbeing is a field ready for wellbeing strategy conversations. Research discoveries featuring every one of these territories show up as: Zits (skin inflammation) are the absolute most basic constant sickness of youths.[10, 11]

KEYWORD: Dermal sticks, Dapsone, heating and congealing method, Franz diffusion cell, FTIR, DSC.

MATERIALS AND METHODS MATERIALS

MATERIAL: Dapsone (Atul Ltd Pharmaceuticals And Intermediates Business, Gujrat Ltd), Hard Paraffin, White Soft Paraffin, Propylene Glycol (Gopaldas Visram And Co.Ltd, Mahape, Ghansoli) Cetostearyl Alcohol, Sodium Lauryl Sulphate, Almond Oil (Shalina Laboratories Pvt.Ltd Mumbai)

PREPARATION OF MEDICATED STICKS: Medicated sticks of dapsone were prepared by heating and congealing. All the ingredients were weighed separately. Hard paraffin, White Soft Paraffin, and Cetostearyl Alcohol were melted according to their decreasing melting points and mixed well to obtain a base melt. In another container the Propylene Glycol, Almond Oil White Petrolatum and propylene glycol were melted together and mixed well to obtain a liquid melt. The base melt was added to the liquid melt with stirring and into this the sodium lauryl Sulphate was added and mixed well. The resultant mixture was cooled to about 37°C and the Drug was incorporated and mixed well to obtain a uniform mixture. The warm mixture was poured into the stick moulds and cooled to get the desired shape of the Medicated sticks. [2, 3]


Fig: Heat and Congealing method

PREFORMULATION EVALUATION:

Solubility, melting point determination was done for drug Dapsone to test its purity and the values were found within the range, then Fourier transform infrared Spectroscopy (FT-IR) was conducted to test the compatibility of the drug with the excipients.

EVALUATION OF DERMASTICKS:

Weight variation:

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 calipers respectively. The average thickness was measured, by observing thickness at three different parts of the stick.[2]

Physical appearance:

The formulated sticks were visually inspected for colour, odour, solubility and appearance and reported.[4]

Melting point: Determination of melting point is important as it is an indication of the limit of safe storage. The melting point of formulated sticks was determined by hot plate method,sticks was kept in the apparatus and firstly observed the product was slowly melted. The above procedure was done 3 times and the melting point was observed in all formulations.[1,8].

Weight Variation: 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 sticks is cylindrical the thickness and length was determined with the help of screw gauge and vernier caliper respectively. The average thickness was measured, by observing thickness at three different parts of the sticks[1,8].

Breaking Point: Breaking point was done to determine the strength of the stick. The stick was held horizontally in a socket inch away from the edge of support. The weight gradually increased by a specific value (10gm) at specific interval of 30 sec and weight at which breaks was considered as the breaking point.[1]

Force of application: It is a test for comparative measurement of the force to be applied for application. A piece of brown paper kept and stick was applied at a 45ºC angle to cover a 1 sq. Inch Area until fully covered. The pressure reading is an indication of force of application.[8,6]

Aging stability: the products were stored in 40ºC for 1 Hrs. various parameters such as bleeding, crystallization of on surface and ease of application were observed.[8]

pH measurement: The small amount of sample was placed on a glass slide and the pH of the formulation was measured using a pH paper at Room temperature and the results were reported.[1]

Uniformity of drug content: for drug content uniformity the stick equivalent to 50 mg of drug was extracted with phosphate buffer pH 7.4 and filtered. The drug content was calculated using the standard calibration curve. The mean percentage was calculated as an average of three determinations.[1]

Softening point (Ring and ball method): The stick sample was inserted into an aluminum ring. Extra mass above and below the orifice was removed using a sharp blade to get a stick tablet into the ring. This was placed in a refrigerator (6ºC) for 10 mins. After removing it from the refrigerator, the ring was fastened onto a stand and a steel ball was delicately placed on the stick tablet. The assembly was dipped into a beaker full of water .Temperature was raised and monitored using a thermometer. Softening point of the stick was the temperature at which both the stick mass and steel ball were loosened and falls to the bottom of the beaker.[1]

Spreadability: Spreadability is defined in terms of time in seconds required taken by the upper slide to slip off the stick placed between the two slides, under certain load. The lesser the time taken for the separation of two slides, the better the Spreadability. take 500 mg of the formulation was stand witched between the two slides, each with dimensions of 6 x 2 cm. Then observed the Spreadability of the time taken by the upper slide to slip off the lower slide was noted.

Spreadability = m × l/t

Where, m=weight tied to upper slide, l=length of the glass slide (6 cm), t= time in sec.[10, 11]

Drug Solubility: solubility test for the drug Dapsone was performed by using various solvents. The solvents include water, methanol, ethanol, acetonitrile and chloroform but it was found that Dapsone was soluble in methanol: water (60:40) Drug solubility studies of Dapsone were achieve in threefold by adding required amounts of drug to water and buffer solutions having different pH (7.4) buffers. The solutions containing flasks were kept on a rotary shaker for 24 h. After 24 h, solutions were determined by using UV spectrophotometer at 303 nm, which was the maximum absorption analyzed prematurely and drug concentrations were calculated.[5,9]

***In vitro* drug diffusion studies [4,6]:**

In vitro drug release studies were studied using a permeation cell. A pre-hydrated cellophane membrane (24 hrs. before use) was fixed to the one end of the glass cylinder. Stick containing one gram of drug was taken in the cell (donor compartment) and then the cell was immersed in a beaker containing 150 ml of drug free phosphate buffer (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 37oC ± 1°C was maintained. Samples (5 ml) of the receptor compartment were withdrawn at specified intervals over a period and analyzed for drug content by measuring the absorbance. The volume of samples withdrawn at each interval was replaced with a fresh quantity of diffusion medium. Cumulative percent of drug released was calculated.

Stability Studies[7]: Short-term stability studies for all the formulations prepared were carried out by storing 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.

RESULT AND DISCUSSION:

Melting Point of dapsone (pure drug)

Standard value is 176-181°C
Practically found at 175°C. (Pubchem dapsone U.S. national library of medicine)

Table no:1. Solubility of Dapsone:

Sr no	Solvent	Solubility
1	Water	Good
2	Methanol	Good
3	Ethanol	Good
4	Phosphate buffer 7.4	Very Good

Table no:2.Composition of Dapsone Dermal stick

Ingredients (10g)	**F1**	**F2**	**F3**	**F4**	**Role Of Ingredients**
Dapsone	0.750	0.750	0.750	0.750	Acne
White Soft Paraffin(ml)	3	3	3	3	Emollient
Micro Crystalline Wax (mg)	0.5	0.5	0.5	0.5	Stiffening Agent
Cetostearyl Alcohol(ml)	1.5	1	1	1.5	Penetration Enhancer
Sodium Lauryl Sulphate (mg)	0.15	0.50	0.15	0.15	Humectant/Penetration Enhancer
Almond Oil(ml)	3	3	3	3	Emollient
Propylene Glycol(ml)	1.10	1.25	1.60	1.10	Humectant
Water	QS	QS	QS	QS	vehicle

Table no:3. Evaluation of medicated sticks (F1-F4)

Formula code	Weight (gm)	Thickness(mm)	Length (cm)	Drug content % dapsone
	Mean ±SD	Mean ±SD	Mean ±SD	
F1	3.00± 0.02	1.1±0.02	3.4±0.02	72.36%
F2	3.00±0.02	1.1±0.02	3.4±0.02	68.46%
F3	2.98±0.02	1.1±0.02	3.4±0.02	65.17%
F4	3.03±0.02	1.1±0.02	3.4±0.02	74.96%

Table no.4: Physical evaluation of medicated sticks (F1-F4)

Sr No	Parameter	F1	F2	F3	F4
1	Color	Creamy	White	Slightly Yellow	White
2	Solubility	Phosphate Buffer 7.4	Phosphate Buffer 7.4	Phosphate Buffer 7.4	Phosphate Buffer 7.4
3	Melting point	48.3ºC	45ºC	47.2ºC	47.6ºC
4	Odour	Odorless	Odorless	Odorless	Odorless
5	Weight Variation	Normal	No	Slightly	Normal
6	P^H	6.8	7	6.5	6.8
7	Spredability	++	+++	+	++
8	Force Of Application	Good	Good	Good	Good
9	Surface Anomalies	Defect	No Defect	Defect	Defect
10	Ageing Stability	No	Yes	No	Yes
11	Breaking Point	30sec	20 Sec	30 Sec	20 Sec
12	Softening Point	39ºC	36ºC	37ºC	37.3ºC
13	Drug release	72.36%	68.46%	65.17%	74.96%

Table no.5: *In-vitro* drug release of dapsone sticks in pH 7.2 phosphate buffer (F1-F2)

Time (min)	% cumulative Drug release			
	F1	F2	F3	F4
0	0	0	0	0
30	3.528	3.4416	2.7888	3.816
60	8.1888	7.4352	6.4272	8.688
120	14.04	12.5808	10.944	14.6928
180	21.0912	18.5664	16.2672	22.2144
240	29.6064	26.6352	22.8672	31.3104
300	39.1824	35.9232	31.8192	41.1264
360	49.6128	45.7872	42.1008	57.888
420	60.6816	56.9088	53.4528	63.44
480	72.3648	68.4672	65.1744	74.96

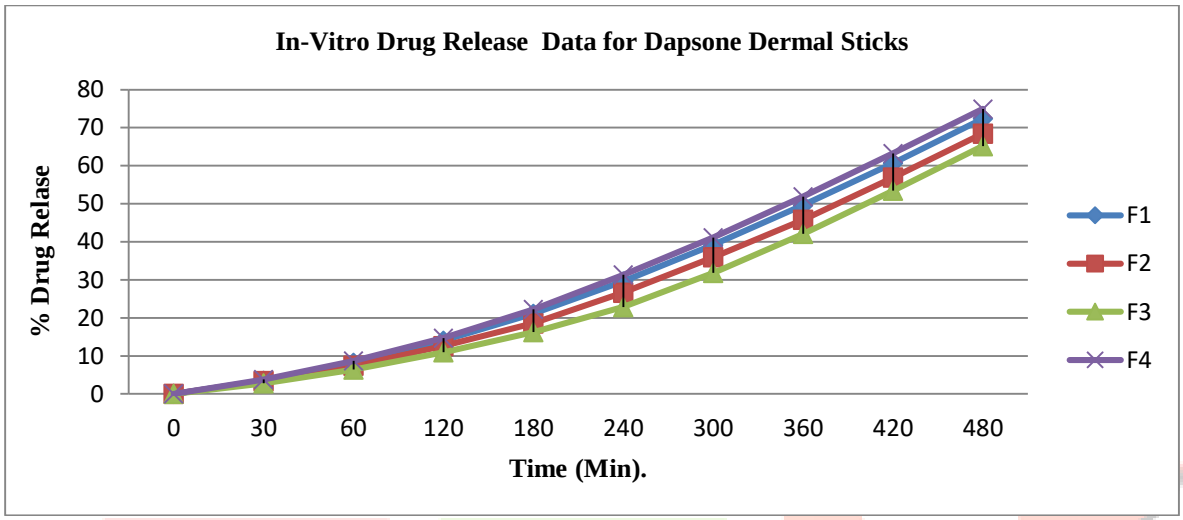
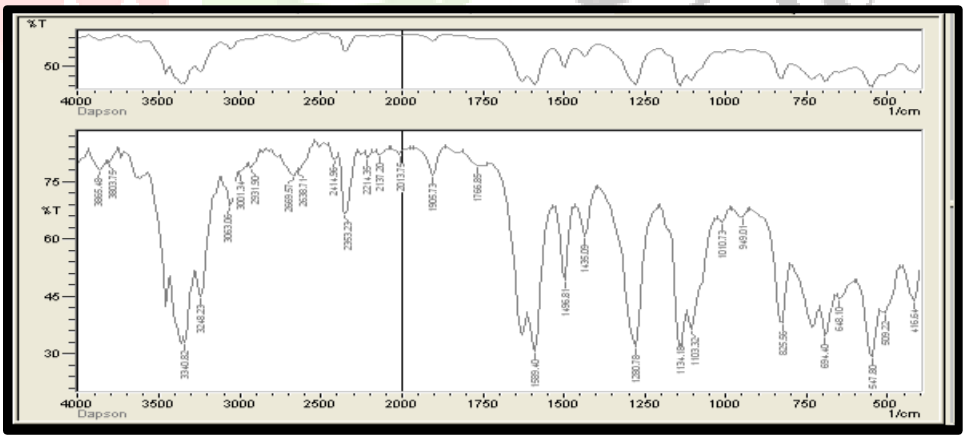
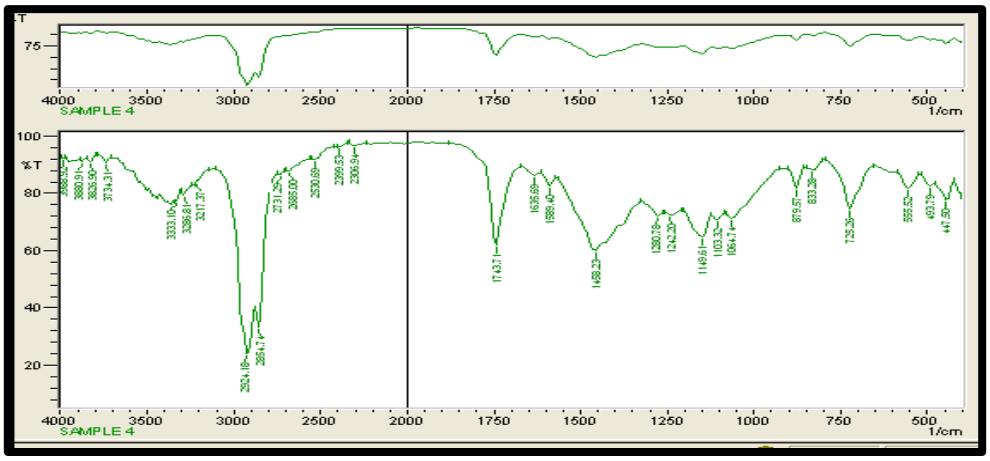


Fig.6: *In-vitro* cumulative percentage drug release Vs. Time profile of formulation (F1-F4) in pH7.4 phosphate buffer.

FTIR SPECTRA OF DAPSONE



FTIR SPECTRA OF FORMULATION 4



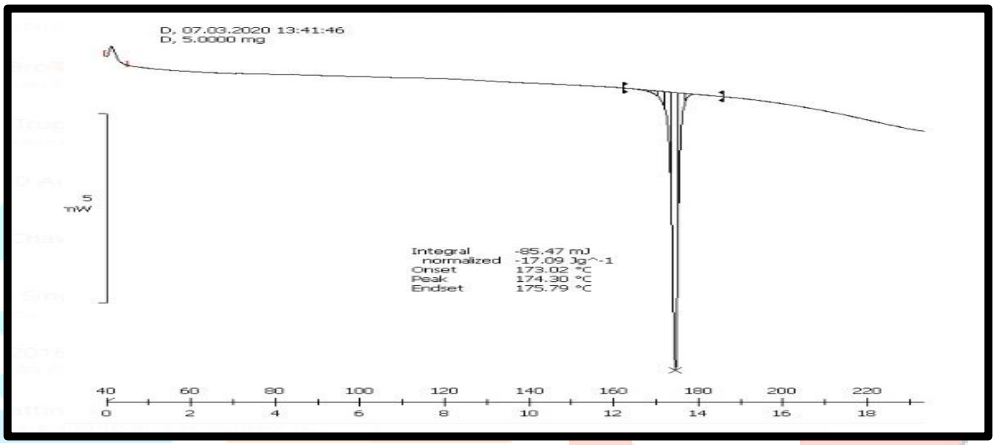


Fig.:Dsc of Dapsone

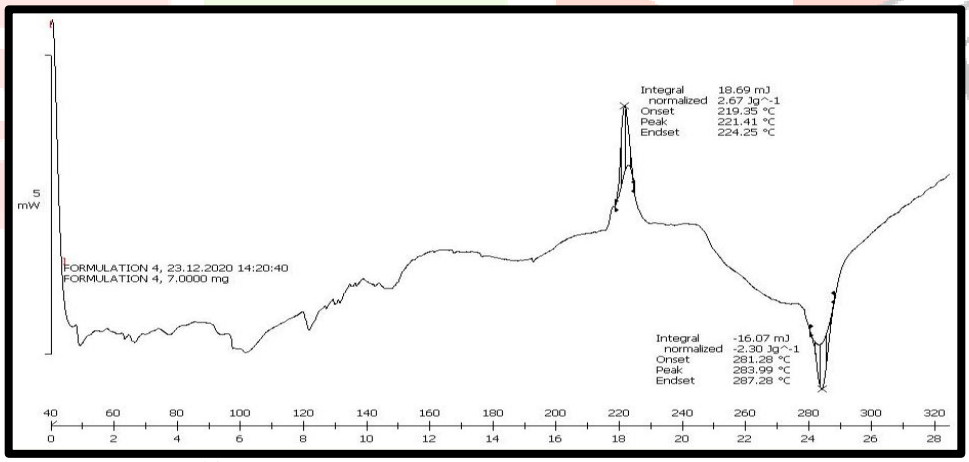


Fig.: DSC of formulation 4

Final Formulation of Dermal Acne Stick

Discussion: Non-medicated sticks of dapsone prepared by heating & congealing method using Cetostearyl alcohol, hard paraffin wax, as stiffening agents. While petroleum is used as an emollient. Propylene glycol and sodium lauryl Sulphate were used as humectant & emulsifying agents. Almond oil & propylene glycol used as a penetration enhancer, and this composition was used for dapsone dermal stick preparation. A total 3 formulations were designed as non-medicated dermal sticks. A total 4 formulations were designed as medicated dermal sticks preparation.

Conclusions: There are following conclusions that can be drawn for anti-acne dermal stick study: The optimum concentration of polymers was found to be 0.5 – 1.5 % for preparation of stick. By using the heating & congealing method the preparation affected the homogeneity and consistency of formulated Stick. After complete, addition of drugs and bases in formulation had satisfactory sticks. Selection and concentration of Bases used directly affected the physical properties of the dermal stick. Melting point of a drug 178ºC was found and wavelength at 307nm.Melting point of an F1 & F2 found to be 48.3ºC & 45ºC Were F3 & F4 found to be 47.6ºC & 47.6ºC Color of a dermal stick was white in color but Formulation F1& F3 shows yellowish color and F2 & F4 formulation shows white in color. Force of application of formulation F1-F4 from that the best result shown in formulation F4 formulation. Surface anomalies or defect parameter in Formulation F1-F4 shows good surface anomalies and there is no defect. Breaking point (Sec) F1 and F3 Shows 30 sec break point as compare to F2 and F4 shows good breaking point i.e.20 sec. Softening point also carried out F1-F4 from this F3 and F4 shows 37ºC &37.3ºC which was best. Weight variation in F1 & F3 was observed but in F2 & F4 it shows slightly change. Spreadability of a formulation F1-F4, hence formulation F4 shows best Spreadability. Formulations F1, F2, and F3 showed satisfactory results in terms of anti- acne potency but F4 formulation shows good results. The % cumulative drug release study was carried out by using Franz diffusion cell with phosphate buffer pH 7.4 hence, F1,F2,F3&F4 formulation shows 72.36% , 68.46%,65.17 % ,74.96 % of drug release calculated at 480 min

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