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FORMULATION AND EVALUATION OF MEDICATED ANALGESIC STICKS

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ABSTRACT

The main objective of this research was to formulate an analgesic drug incorporated in topically used sticks, prepared using suitable ointment bases with varied concentrations of waxes, lubricants, surfactants, etc. and incorporation of medicament in the optimized formula by heating and congealing process. Indomethacin was the drug of choice used because; this drug if used orally has a lot of side effects which has to be reduced. The main purpose of this formulation was to dispense medicated derma sticks to the patients, specially suffering from rheumatoid arthritis, as Indomethacin is effective in treating rheumatoid arthritis. Here the patients can apply the medicated derma stick at the site required and as per the need without messing their hands and without tissue toxicity. The medicated sticks were prepared using various other bases but, due to the stability problems the ointment bases were used. 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 prehydrated cellophane membrane for 160 minutes in pH 7.2 phosphate buffer and Stability studies were conducted for a period of 3 weeks and FT-IR Spectral analysis was conducted.

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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 available for the treatment of pain such as headache, muscle strain, bruising, or arthritis, have several disadvantages like greasiness, inconvenient to store and requires applicator or use of fingertip, which may lead to contamination.[1] Therefore the present work was done to overcome all these disadvantages. The term Analgesics encompasses a class of drugs that are designed to relieve pain without causing the loss of consciousness or any member of the group of drugs used to achieve analgesia, relief from pain. Analgesic drugs act on the peripheral nervous systems and central nervous systems. Analgesics can be used for either short-term or long-term relief of severe pain.[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 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, immediate onset of action, reduced dosage regimen and economy, One such approach is medicated sticks. Objective of the present work was to develop a NDDS of Indomethacin prepared by heating and congealing method a convenient model to use by patients.

MATERIALS AND METHODS

MATERIALS

Indomethacin (Yarrow Chem Products, Delhi), Cetostearyl alcohol (Hi-Media Laboratories pvt.ltd. Mumbai), White soft paraffins (NICE chemicals pvt.ltd. Kochi), White bees wax (SD Fine chemicals pvt.ltd, Boisar), Ethanol (ChangshuYangyuan Chemical, China).

PREPARATION OF MEDICATED STICKS

Medicated sticks of Indomethacin were prepared by heating and congealing. All the ingredients were weighed separately. The White Beeswax and Cetostearyl Alcohol were melted according to their decreasing melting points and mixed well to obtain a base melt. In another container the 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. [3]

PREFORMULATION EVALUATION

Solubility, melting point determination was done for drug indomethacin 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 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. [4]

Physical appearance:

The formulated sticks were visually inspected for colour, odour, solubility and appearance and reported. [6]

Melting point:

The melting point of formulated stick was determined by capillary tube method, the capillary tube was filled and keep in the capillary apparatus and firstly observed that the product was slowly melted. After sometimes observed product was completely melted. The above procedure was done in 3 times and the melting point ratio was observed in all formulations.

Uniformity of drug content:

For drug content uniformity the stick equivalent to 50 mg of drug was extracted with ethanol and filtered. The drug content was determined by measuring the absorbance, after appropriate dilution with ethanol. The drug content was calculated using the standard calibration curve. The mean percent was calculated as an average of three determinations. [5]

Breaking point:

Breaking point was done to determine the strength of the Medicated stick. The stick was held horizontally in a socket inch away from the edge of support. The weight was gradually increased by a specific value (10 gm) at specific interval of 30 second and the weight at which the stick breaks was considered as the breaking point. [6]

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.

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 (6^0C) for 10mins. After removing it from the refrigerator, the ring was fastened onto a stand and a steel ball was delicately placed on the stick tablet. This 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.

In vitro drug diffusion studies:

In vitro drug release studies was studied using 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 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 37^oC ± 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 sample withdrawn at each interval was replaced with a fresh quantity of diffusion medium. Cumulative percent of drug released was calculated. [(4)]

Spread ability:

Spread ability is a term expressed to denote the extent of area to which the topical application spreads on application to skin on the affected parts. The therapeutic efficiency of the formulation also depends upon its spreading value. Hence, determination of spread ability is very important in evaluating topical application characteristics. For the determination of spread ability, the sticks was evaluated and ranked according to this grading: No spread ability (0), low spread ability (+), average spread ability (++), high spread ability (+++). [(7)]

Stability Studies:

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. [(7)]

RESULTS AND DISCUSSION

TABLE NO. 1: MELTING POINT OF INDOMETHACIN (PURE DRUG).

SI. No.	Actual melting point	Observed melting point °C
1		157
2	158 °C	158
3		158
	Average melting point	158

TABLE NO. 2: SOLUBILITY OF INDOMETHACIN.

Sl. no	Solvent	Solubility mg/ml	Observation
1	Ethanol	25 mg/ml	Clear solution
2	Acetone	42 mg/ml	Clear yellow solution
3	Chloroform	53 mg/ml	Clear yellow solution
4	Water	Insoluble	White precipitate

TABLE NO. 3: COMPOSITION OF INDOMETHACIN STICKS (F1-F4).

Sl. no	INGREDIENTS	QUANTITY (5 gm)			
		F 1	F2	F3	F4
1	DRUG	0.1 g	0.1 g	0.1 g	0.1 g
2	CETOSTERYL ALCOHOL	10568 g	1.47 g	1.66 g	2.058 g
3	WHITE SOFT PARAFFIN	20254 g	1.421 g	1.47 g	2.082 g
4	PROPYLEN GLYCOL	0.588 ml	0.98 ml	0.98 ml	0.612 ml
5	SODIUM LAURYL SULPHATE	0.49 g	0.049 g	0.049 g	0.147 g
6	WHITE BEES WAX	-	0.98 g	0.735 g	-

TABLE NO. 4: EVALUATION OF MEDICATED STICKS (F1-F4).

Formulation code	Medicated stick			Drug content (%) Indomethacin
	Weight (gm)	Thickness (mm)	Length (cm	
	Mean ± SD	Mean ±SD	Mean ± SD	
F1	3.98± 0.02	1.4± 0.02	4± 0.02	59.95
F2	4± 0.02	1.4± 0.02	4± 0.02	46.55
F3	3.98± 0.02	1.4± 0.02	4± 0.02	56.73
F4	3.98± 0.02	1.4± 0.02	4± 0.02	57.68

TABLE NO. 5: PHYSICAL EVALUATION OF MEDICATED STICKS (F1-F4).

Sl no.	Evaluation parameter	Inference			
		F1	F2	F3	F4
1	Color	Pale yellow	Pale yellow	Pale yellow	Pale yellow
2	pH	5.5	5.5	5.5	5.5
3	Melting point	48.3°C	43°C	47.3°C	47.6°C
4	Breaking point	30	25	30	30
5	Force of application	Good	Good	Good	Good
6	Surface anomalies	No defect	No defect	No defect	No defect
7	Solubility test	Ethanol, pH 7.2 buffer	Ethanol, pH 7.2 buffer	Ethanol, pH 7.2 buffer	Ethanol, pH 7.2 buffer
8	Odour	Odorless	Odorless	Odorless	Odorless
9	Appearance	Good	Good	Good	Good
10	Softening point	39°C	36°C	37°C	37.3°C
11	Spread ability	+++	++	++	+++

TABLE NO. 6: IN-VITRO DRUG RELEASE OF INDOMETHACIN STICKS IN PH 7.2 PHOSPHATE BUFFER (F1-F4).

Sl.no	Time (min)	% cumulative Drug release				
		F1	f2	F3	F4	Indo cream
1	0	0	0	0	0	0
2	20	15.01	16.44	12.13	13.6	15.1
3	40	20.217	38.11	23.12	28.11	26.9
4	60	30.27	39.01	31.18	42.32	39.2
5	80	52.32	43.47	47.66	50.13	59.1
6	100	64.589	48.19	52.21	57.12	72.1
7	120	68.98	53.891	57.18	64.33	84.6
8	140	74.34	61.07	63.3	71.21	90.3
9	160	76.883	66.2	69.91	75.33	96.1

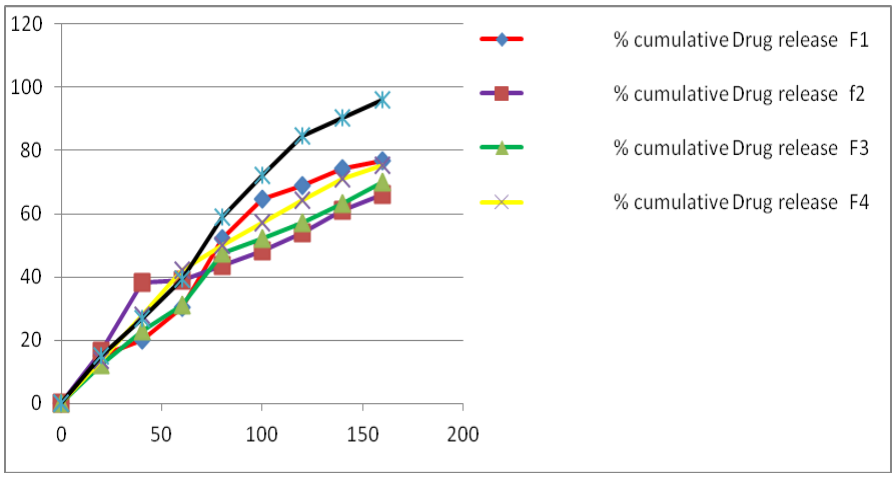

FIGURE-1: IN VITRO CUMULATIVE PERCENT DRUG RELEASE VS. TIME PROFILES OF FORMULATIONS (F1-F4) IN PH 7.2 PHOSPHATE BUFFER.

STABILITY STUDIES RESULTS OF FORMULATION (F1-F4).

TABLE NO. 7: DRUG RECONTENT UNIFORMITY FOR FORMULATION (F1-F4), DURING STABILITY STUDIES.

Sl.no	Formulation code	Condition at 27±2°C			
		initial	1st week	2nd week	3rd week
1	F1	59.95	59.08	59.08	59
2	F2	46.55	46.55	46.51	46.43
3	F3	56.73	56.3	56.20	56.13
4	F4	57.68	57.60	57.60	57.51

TABLE NO. 8: PHYSICAL APPEARANCE FOR FORMULATION (F1-F4), DURING STABILITY STUDIES.

Sl.no	Formulation code	Physical appearance			
		Initial	1st week	2nd week	3rd week
1	F1	Pale yellow	Pale yellow	Pale yellow	Buff colour
2	F2	Pale yellow	Pale yellow	Pale yellow	Buff colour
3	F3	Pale yellow	Pale yellow	Buff colour	Buff colour
4	F4	Pale yellow	Pale yellow	Pale yellow	Buff colour

FT-IR SPECTRA OF INDOMETHACIN AND FORMULATION (F1-F4).

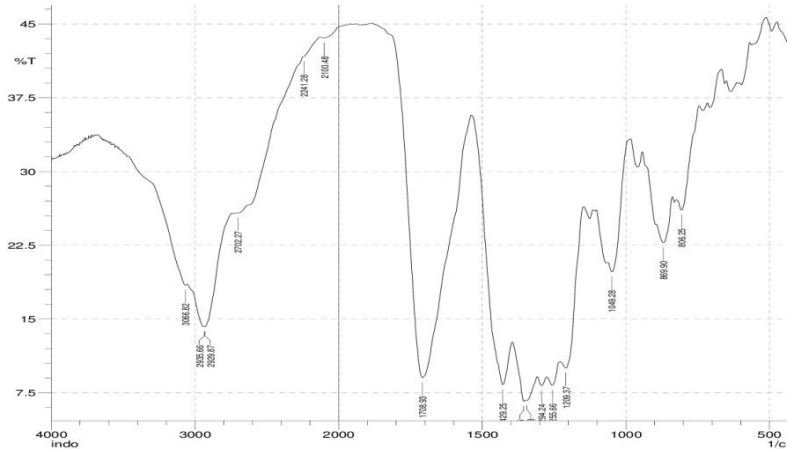

FIGURE-2: FT-IR SPECTRA OF INDOMETHACIN (PURE DRUG).

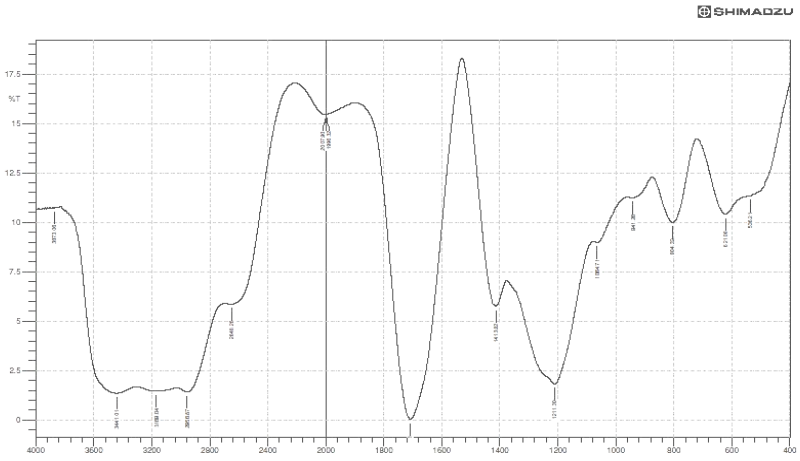

FIGURE-3: IR SPECTRA OF INDOMETHACIN DERMA STICK (I).

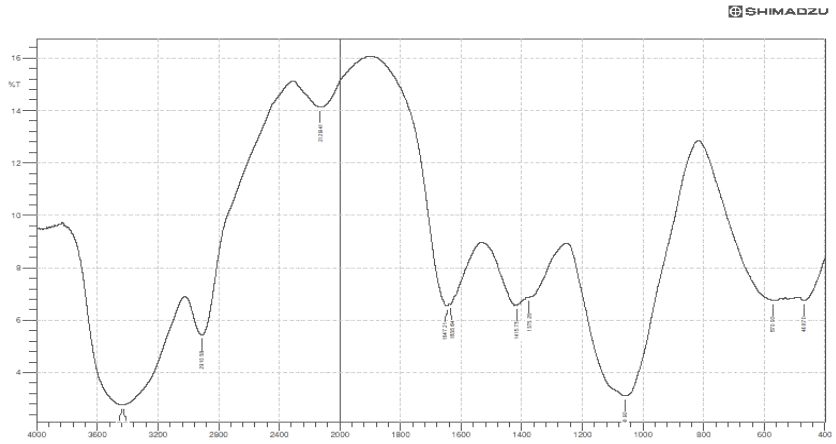

FIGURE-4: IR SPECTRA OF INDOMETHACIN DERMA STICK (II).

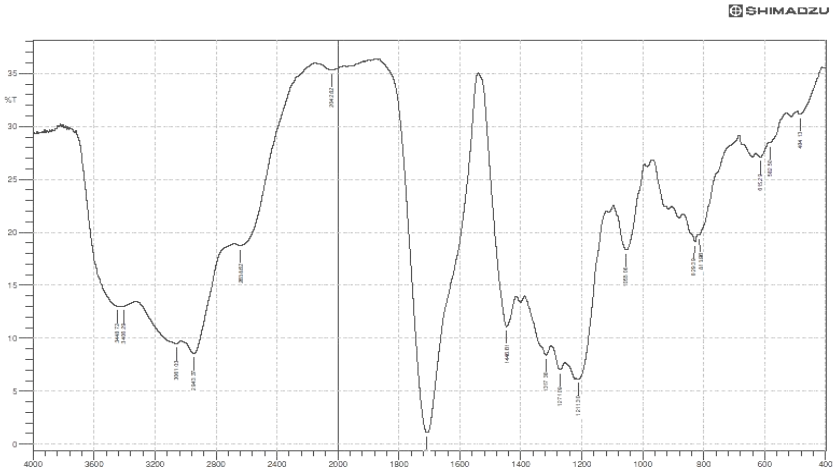

FIGURE-5: IR SPECTRA OF INDOMETHACIN DERMA STICK (III).

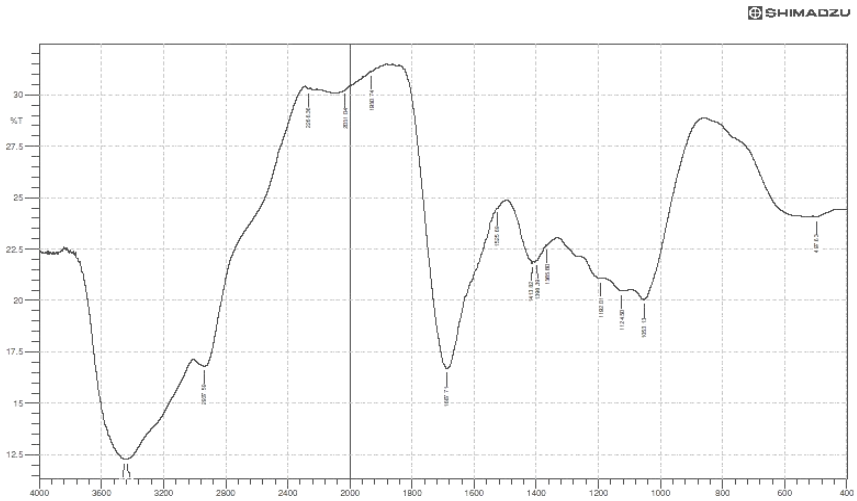

FIGURE-6: IR SPECTRA OF INDOMETHACIN DERMA STICK (IV).

DISCUSSION

Analgesic medicated sticks of indomethacin were prepared by using white bees wax as a vehicle, stiffening agent, white soft paraffin as an emollient, Cetostearyl alcohol as a main base a vehicle that imparts consistency, propylene glycol a vehicle and humectant and sodium lauryl sulphate as a surfactant ant and a suspending agent. A total number of four (F1-F4) formulations were prepared by heating and congealing method. The Preformulation studies such as solubility, melting point and FT-IR studies were done to identify the purity of drug indomethacin and ensure the compatibility of drug with the selected excipients, the results were found to be within prescribed limits. the data obtained from physico- chemical parameters such as Color , melting point, pH, Breaking point, Force of application, Surface anomalies, Solubility test, Odour, Appearance, Softening point, drug content uniformity, in-vitro drug diffusion were good.

CONCLUSIONS

The objective of the present study was to design and formulate medicated sticks of indomethacin an analgesic drug which is an non selective inhibitor of cyclooxygenases COX1 and 2 that participate in prostaglandin synthesis from arachidonic acid, to implement a design of experimental principles an developing a formulationhaving better stability and better patient compliance. Formulated analgesic medicated stick was evaluated for physical parameters like softening point, melting point, Surface anomalies, Weight variation, Spread ability, In-vitro drug diffusion studies, Uniformity of drug content, Breaking point. Microbial growth, pH, etc. and obtained results were in the acceptable limits. The formulated medicated stick containing analgesic was found to be easier and simpler, to produce stable analgesic medicated stick.

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