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Formulation and Evaluation of Transdermal Patch of Iodine as Ladies Bindi

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Abstract : Iodine is daily dietary essential element. It is well absorbed from orally but oral consumption are food source depending and sometimes not meet daily requirement And the deficiency of Iodine Occur , Iodine is more important in pregnant women and need of iodine is also more in pregnancy Hence, I attempt was made to prepare and evaluate A transdermal patch containing iodine for ladies as a model drug by solvent casting method using hydrophilic ,and lipophillic polymers. Which has both properties as Make up (Bindi) as well as Pharmaceutical patch to deliver Iodine to Females; Various formulations were prepared by using Ethyl cellulose, polyvinyl pyrrolidone as film former and Propylene glycol as plasticizer as well as penetration enhancer .The ,prepared transdermal patches were evaluated for their physicochemical and mechanical parameters. A 3^2 full factorial design was applied to the formulations containing different concentration of polymer and plasticizer combination. From factorial design batches (F1-F9) the batches with higher drug release and higher permiablity were considered as optimized batches. The results of *In-vitro* study indicates that the formulation prepared by using ethyl cellulose, polyvinylpyrrlidone, propylene glycol for suitable proportion exhibited higher release of drug ,and improved *In-vitro* permeation through Rat skin than the formulation prepared by using ethyl cellulose polyvinylpyrrlidone, propylene glycol .Finally it can be concluded that the transdermal drug delivery of Iodine can be achieved through a transdermal patch formulated by using ethyl cellulose polyvinylpyrrlidone and propylene glycol.
Keywords : Ethyl cellulose, polyvinylpyrrolidone, propylene glycol, *In-vitro* drug release, *In-vitro*permeation.

Introduction:

Iodine is more important in pregnant women and Lactating Lady and need of iodine is also more in pregnancy and in Lactation Hence, I attempt was made to prepare and evaluate A transdermal patch containing iodine for ladies as a model drug by solvent casting method using hydrophilic ,and lipophillic polymers. Which has both properties as Make up (Bindi) as well as Pharmaceutical patch to deliver Iodine to Females. Various formulations were prepared by using Ethyl cellulose, polyvinyl pyrrolidone as film former and Propylene glycol as plasticizer as well as penetration enhancer . A 3^2 full factorial design was applied to the formulations containing different concentration of polymer and plasticizer combination. From factorial design batches (F1-F9) the batches with higher drug release and higher permiablity were considered as optimized batches. The ,prepared transdermal patches were evaluated for their physicochemical and mechanical parameters such as physical appearance, surface pH, thickness and weight uniformity, drug content uniformity, folding endurance,

*In-vitro*drug release, *In-vitro* permeation and invitro skin irritation study. Most of the iodine in nature is found in marine sediment in the form of iodine salts. Iodine is an essential trace element required for the synthesis of the thyroid hormones, thyroxine T4 and triiodothyronine T3. The human body contains 15-20 mg of iodine with 70-80% being located in the thyroid gland. Iodine that is taken up in the thyroid gland is oxidized by hydrogen peroxide and thyroid peroxidase. The oxidized active iodine is attached to a glycoprotein called thyroglobulin. The active iodine reacts with the tyrosine components of thyroglobulin to form 3-monoiodotyrosine MITs and 3,5diiodotyrosine DITs. The MITs and DITs are coupled to form triiodothyronine T3 and thyroxine T4 residues on the thyroglobulin. The MITs and DITs couple to form the active thyroid hormones, T3 and T4.

This prepared patch have a number of advantages as below:

The feeling of patient and medicine is eliminated in this formulation because the formulation is a Bindi which is wear by the Females On Daily basis.

Material and Methods:

Table No. 7.1: List of Chemicals

Sr. No.	Name of the Ingredients	Category	Manufacturer / supplier
1	Iodine.	Drug	Mylochem Lab.
2	Ethyl Cellulose.	Polymer	Meck Ltd.
3	Propylene Glycol	Plasticizer	Merck Ltd.
4	Polyvinylpyrrolidone	Polymer.	Merck Ltd.

Table No. 7.2: List of Instruments

Sr. No.	Name of the Instrument	Model/Make
1	Analytical weighing balance	LC/GC (AXIS)
2	UV spectrophotometer	Shimadzu 2450 , Japan
3	ATR spectrophotometer	Shimadzu, Japan
4	DSC	Mettler Toledo straw 10.00
5	Magnetic Stirrer	RemiEquipments, Mumbai.
6	Sonicator	Citizen.
7	Hot Air Oven	Thermolab, Mumbai
9	USP Dissolution Apparatus	Lab India DS 8000
10	Digital PH meter	Hanna Instruments
11	Stability chamber	Thermolab, Mumbai.
12	Franz Diffusion Apparatus	Orchid

Formulation and Evaluation of Transdermal Patches:

A] Dose calculation:

The drug to be loaded in patch was determined by the dose of the drug and the loading in the petri plate was determined by the area of petri plate.

B] Role of the casting surface:

It was evaluated on the basis of how is affected the patch forming capacity, appearance of the film, easiness to remove the patch from the casting surface.

General Procedure for Preparation of Iodine Transdermal patch:

The Iodine Transdermal patches were prepared by solvent casting technique. Various polymers were used as a film forming polymer.

1. Accurately weighed quantity of polymer was dissolved in specified quantity of suitable solvent. Weighed quantity of plasticizer was added to the above solution and dissolved by using magnetic stirrer.
2. Weighed quantity of Iodine was dissolved in 10 ml of appropriate solvent, separately.
3. Solution of 2% Iodine was added to previously prepared solution of polymer and plasticizer, and mixed thoroughly.
4. The above solution kept aside for 1 day for removal of air bubbles. Then casted on petriplate and dried overnight to form the film.
5. Then the film was carefully removed and cut into suitable size i.e. 2cm x 2cm.

Evaluation Parameters:

1) Weight of Patch:

Transdermal patches were weighed on analytical balance and average weight was determined for each film. It is desirable that films should have nearly constant weight. It is useful to ensure that a film contains the proper amount of excipients and API.

2) Thicknesses of Patch:

The thickness of the patch was measured by micrometer screw gauge at five different places; an average of three values was calculated**.** This is essential to ascertain uniformity in the thickness of the film this is directly related to the accuracy of dose in the film.

3) Surface pH:

Patches were kept in glass tubes containing 10 ml phosphate buffer (pH -7.4) and the pH of the surface measured after 1, 2, 3, 4, 5, 6, 7 and 8 hours by placing the tip of the glass microelectrode of a digital pH meter close to the surface of the patch and allowing it to equilibrate for 1 min prior to recording.

4) Folding Endurance:

Folding endurance of the patch is essential to study the elasticity of the film during storage and handling. The folding endurance of the patch was determined by repeatedly folding one film at the same place till it break. This is considered to reveal good film properties. A film (2 X 2 cm) was cut evenly and repeatedly folded at the same place till it breaks. All determinations were performed in triplicate.

5) Swelling and Erosion:

Swelling and erosion of patches were determined under conditions identical to those for dissolution tests. The degree of swelling (water uptake) and extent of erosion (mass loss) were determined according to the equations:

$$\text{Degree of swelling} = \frac{\text{Wet weight - Original dry weight}}{\text{Original dry weight}}$$

$$\% \text{ Erosion} = \frac{\text{Original weight - Remaining dry Weight}}{\text{Original weight}} \times 100$$

6) Assay of Iodine Patch:

A complete patch from petriplate was cut in to2*2 pieces and crushed in mortar pestle and dissolved in phosphate buffer pH 7.4 with continuous agitation. Then contents were filtered through Whatman filter paper into volumetric flask. After appropriate dilution with phosphate buffer pH 7.4, solutions were analysed by

determination of absorbance at 226nm (UV 2450 spectrophotometer) against a solvent blank. Drug content was estimated from a calibration curve.

7) Content Uniformity:

Drug content was determined by dissolving the film containing 2 mg of drug in 100 ml phosphate buffer pH 7.4 to get 20 µg/ml solutions. An aliquot of 1ml sample was withdrawn and diluted to 10 ml with water. Then solution was filtered through whatman filter paper and analyzed by UV- spectrophotometer at λ max of drug. Content uniformity studies were carried out in triplicates for each batch of the film.

8) *In-Vitro* Drug Release:

Patches were firmly secured in beaker (250ml) placed on magnetic stirrer and 100 ml phosphate buffer saline (PBS pH 7.4) added as the dissolution medium. At specified times (1, 2, 3, 4, 5, 6, 7, 8 hours) 5ml aliquots were removed using a syringe and replaced with equal volumes of fresh PBS to maintain the total volume. Samples were filtered through whatman filter paper and concentration of Iodine determined by measuring absorbance at 226 nm.

9) *In-vitro* Permeability:

The rate and extent of Transdermal permeation of Iodine through the mice skin was determined using Franz diffusion cell. Briefly, the receptor compartment (10 ml) was filled with PBS pH 7.4 at 37.0^0C and stirred at 50 RPM. The patch was sandwiched between the donar and acceptor compartment of the diffusion cell on Swiss albino mice skin the Aliquots (3 ml) of the receptor medium withdrawn at regular intervals(1, 2, 3, 4, 5, 6, 7 and 8 hours) and replaced immediately with equal volumes of PBS pH 7.4 The amount of Iodine released in to the receptor medium was determined by measurement of absorption at 226 nm against a blank.

C] Screening of polymers for preparation of transdermal patch: [1,2,3,4]

Following polymers were checked for film forming ability, polymers are weighed in correct proportions and dissolve in suitable solvent by using magnetic stirrer, and solution were kept for some time for removing air bubble. Polymer solution were spread on surface (glass/ Teflon) and kept for drying in hot air oven for 24 hrs. Film was separated from surface and evaluated for film forming capacity, appearance. From the result obtained polymers were selected for further study.

Table No.9.1: Formulation Batches of Polymers Screening

Ingredients	**P1**	**P2**	**P3**	**P4**	**P5**
PVP K-30 (g)	2.0				
E C (g)		3.0			
HPMC K-15 (g)			2.0		
Chitosan (g)				3.0	
Eudragit S-100 (g)					4.0
Propylene Glycol (ml)	3.0	3.0	3.0	3.0	3.0
Solvent (ml)	20.0	20.0	20.0	20.0	20.0

D] Screening of plasticizer for preparation of transdermal patch.

Table No. 9.2: Formulation Batches of plasticizer Screening

Ingredients	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**
n-di-pthalate. (ml)	1.0	1.0	1.0			
HPMC K-15 (g)				1.0	1.0	1.0
Glycerol (ml)	2.0			2.0		
PEG (ml)		2.0			2.0	
Propylene Glycol (ml)			2.0			2.0
Solvent (ml)	20.0	20.0	20.0	20.0	20.0	20.0

Table No.9.3: Limit for Optimization

Formulation Factor	X1	X2	X3	Levels
Ethyl cellulose(gm)	3.0	3.0	3.0	1, 1, 1.
Polyvinylpyrrlidone(gm)	1.0	2.0	3.0	-1, 0, +1
Propylene glycol.(ml)	3.0	4.0	5.0	-1, 0 +1

Table No.9.4: Actual Formulation Design of F1 to F9 Formulation

Formulation Ingredients	Formulation Codes								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ethyl cellulose (g)	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Polyvinyl pyrrolidone (g)	1.0	2.0	3.0	1.0	2.0	3.0	1.0	2.0	3.0
Propylene glycol (ml)	3.0	4.0	5.0	3.0	4.0	5.0	3.0	4.0	5.0

Table no.9.6. Skin Irritation Scores Following Transdermal Patch Administration.

Sr No	Iodine patch -F7	Iodine Patch -F7	Formalin 0.8%.	Formalin 0.8%	Control Group.	Control Group.
Time (hr).	Erythema	Edema	Erythema	Edema	Erythema	0
1	0	0	2	2	0	0
2	0	0	1	1	0	0
3	0	0	1	0	0	0
4	0	0	2	2	0	0
5	0	0	2	1	0	0
6	1	0	2	1	0	0
7	0	0	1	2	0	0

Fig:Iodine patch Applied for skin irritation Study.

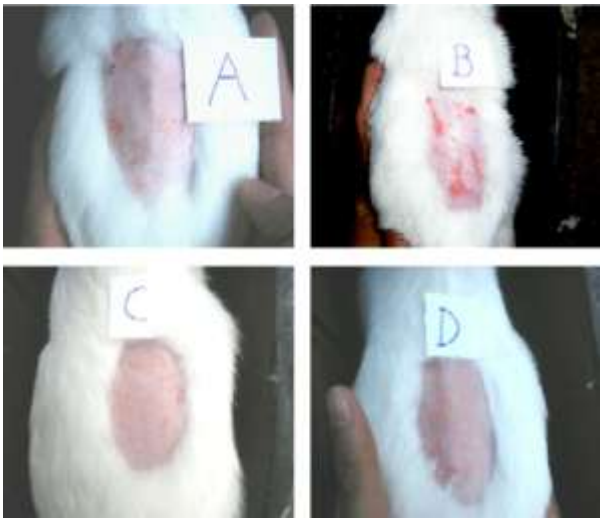


Fig:Before Patch:

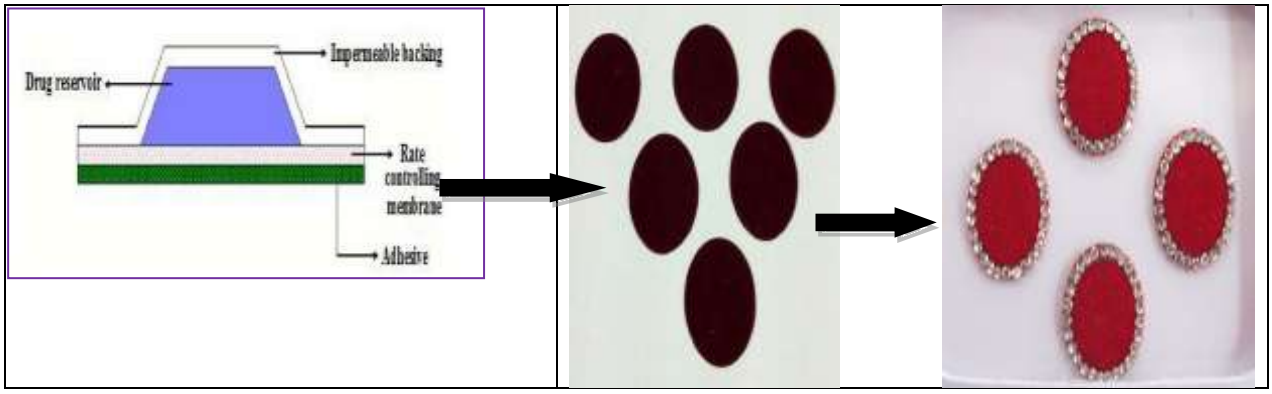


Fig: Patch to (Patch + Bindi transformation)

Invivo Study of Iodine Transdermal patch.

Procedure:

In Vivo Studies The animals used for in vivo experiments were adult male Wistar albino rats (230-250 g) procured from the animal house of MVP Samaj College of Pharmacy , Nasik India). The animals were kept under standard laboratory conditions, at 25 ± 1-C and 55 ± 5% relative humidity with a 12-hour light/dark cycle. The animals were housed in polypropylene cages, 4 per cage, with free access to a standard laboratory diet (Lipton Feed, Mumbai, India) and of the institutional animal ethics committee were followed for in vivo experiments Wistar albino rats were used as the animal models for the bioavailability studies. The animals were selected after superficial examination of the skin surface for abnormalities. Only rats weighing between 230 and 250 g were selected for the study. About 10 cm2 of skin was shaved on the dorsal side. Before application of the patches, rats were kept under observation for 24 hours for any untoward effects of shaving; they were fasted over this period. The rats were divided into 4 groups (n = 6). Group I was administered Iodine by injection (2 ml), group II received transdermal patch F7, . The blood samples were withdrawn at different time intervals (2, 4, 6 , 8, hours). Plasma samples were separated by centrifugation and stored in vials at –70-C until they were analyzed. The plasma iodine concentration was measured according to the Reverse Phase-High Performance Liquid Chromatography (RP-HPLC) method10 with a slight modification. The plasma samples were made alkaline by adding 1N NaOH (50 µL) and extracted with buffer 7.4 PH (0.5 mL). The analytes were back-extracted into 0.2 ml (0.4) of analytes were injected into the RPHPLC system. The chromatographic assembly consisted of a model LC-10A Liquid Chromatograph (Shimadzu, Japan), a Rheodyne 7125injector, and a model RF-10A fluorometry detector set at an excitation wavelength of 228 nm with a 320-nm emission filter. The column used was (5 µm, 150 × 20 mm) C18 base-deactivated. The binary mobile phase consisted of (1) 20 mM pH 7.4 phosphate buffer, and (2) a mixture of methanol, acetonitrile, and isopropanol (7:2:1).The starting mobile phase composition was 31%of mobile phase (2) and increased to 47% in 8 minutes. This percentage was held for 3 minutes; then, the composition returned to initial conditions in 12 minutes.

Results and Discussion:

Preformulation Studies::

1] Description:

Table No.10.1: Description of Iodine.

Identification Test	Reported Standard	Observed Result
Appearance	Crystalline	Crystalline
Colour	Black to Violet	Black to Violet
Odour	Charcterstics	Charactrstics

2] Solubility

Table No. 10.2: Solubility of Iodine.

Solvent	Observed Solubility
Water	12.05 mg/ml
Ethanol	34.14 mg/ml
Phosphate buffer pH 7.4	13.35 mg/ml

3] Melting Point:

Table No. 10.3: Melting Point of Iodine.

Sr. No	Method	M.P. Reported	M.P. Observed
1	Digital melting Point Meter	113.7^0C	$114C^0$
2	DSC	114C	$114C^0$

Formulation of Iodine Transdermal Patches:

1] Dose Calculation:

Diameter of the Petri plate: 9.2 cm. = 9.2\2 = Radius = 4.1
Area of the plate: 16.66 cm^2.
Radius- 4.1 cm
No. of 2 cm^2 films presented in whole plate: 18
Total patch contain 8.5 mg of Iodine
So, 18 each Patch contain 0.5 mg of Iodine

The amount of iodine loaded to Total Patch. = 8.5 mg.

2] Role of casting surface:

The films cast in the Petri plates showed better films forming capacity, appearance than the films cast in the plastic plates. Films were easy to remove from the Petri plates.

3] Trials Batches of Polymers Screening for Preparation of Patch:

Table No. 10.9: Trials Batches of Polymers Screening for Preparation of Patch

Sr. Code.	Polymer Used	Film forming Capacity	Appearance
P1	PVP K 30	Good	Semitransparent
P2	PVA	Good	Semitransparent
P3	Ethyl Cellulose.	Excellence	Transparent
P4	PVP	Excellence	Transparent
P5	Chitosan	Good	Semitransperent.
P6	Eudragit S-100	Good	Semitransparent

Appearance of films of PVP K30, PVA and Eudragit S-100,Chitosan were found to be good film forming capacity but semi-transparent and their texture was found to be rough.

Ethyl cellulose and PVP showed the desirable film forming capacity and appearance as transparent. Hence Ethyl Cellulose and PVP were selected for further study.

4] Trials of Plasticizer Screening for Preparation of Patch:

F1 to F2 formulations were prepared by using Ethyl Cellulose, And PVP polymers using different plasticizers such as Glycerol, PEG 400 and Propylene glycol. All these films were evaluated for appearance and Folding endurance shown in Table no. 10.10

Table No. 10..10: Trials Batches of Plasticizer Screening for Preparation of Patch

Formulation code	Polymer and Plasticizer	Appearance	Folding Endurance
S 1	EC +PVP+ Glycerol	Transparent, sticky	140
S 2	EC+PVP+ PEG 400	Transparent, sticky	144
S 3	EC+PVP+ + PG	Transparent	156
S 4	HPMC + n-di-Pthalate.	Transparent, sticky	115

Evaluation of Iodine Transdermal Patches:

Evaluation Parameters:

Table No.10.14: Evaluation Parameters of all formulations (F1-F9)

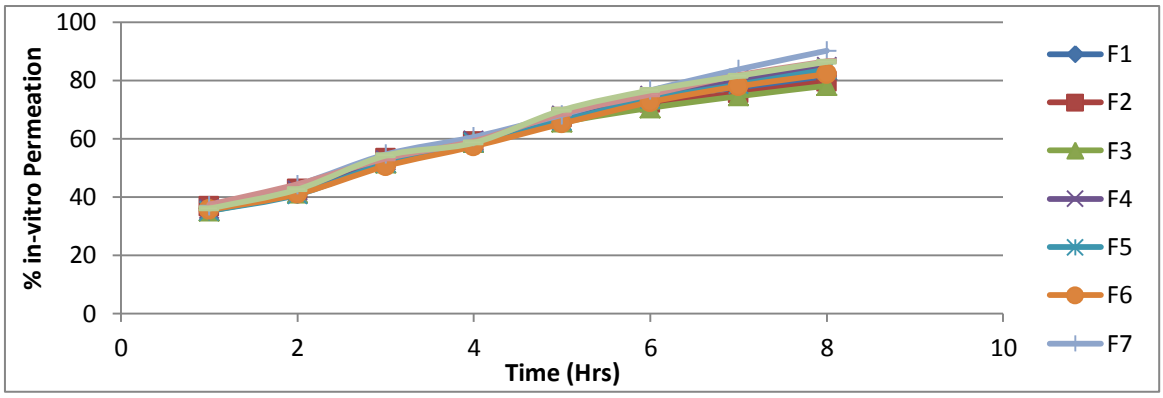
Formulation Code	Average Weight (mg)	Thickness (mm)	Surface pH (After8 hrs)	Folding Endurance	Degree of Swelling	% Erosion
F1	35.0± 0.1	0.49±0.04	6.8±0.1	135±5	2.0±0.3	7.54±0.35
F2	52.4±0.3	0.50±0.03	6.8±0.2	138±6	2.1±0.4	7.59±0.42
F3	53.0±0.3	0.48±0.04	6.8±0.2	141±4	2.38±0.3	10.32±0.12
F4	36.4±0.2	0.51±0.04	7.0±0.3	151±3	2.51±0.2	16.29±0.15
F5	42.2±0.1	0.50±0.03	6.8±0.1	155±5	2.29±0.4	15.66±0.35
F6	48.9±0.2	0.52±0.03	6.8±0.2	159±3	3.71±0.3	18.70±0.34
F7	38.3±0.2	0.54±0.05	6.8±0.1	162±6	2.85±0.3	18.04±0.41
F8	48.6±0.1	0.55±0.04	6.8±0.2	165±7	2.74±0.2	15.17±0.31
F9	83.0±0.1	0.55±0.03	6.8±0.3	170±6	3.24±0.3	±0.22

*All values are mean ± SD, (n=3)

Table No.10.15: *In-vitro* Evaluation Parameters of all formulations (F1-F9)

Formulation Code	%Drug Release	% Drug Content	Content Uniformity (mg)
F1	98.74±0.31	97.84±0.54	3.98±0.05
F2	98.35±0.56	97.47±0.45	3.97±0.05
F3	98.07±0.42	98.21±0.23	3.93±0.04
F4	98.03±0.65	97.84±0.64	3.91±0.02
F5	98.39±0.58	98.95±0.49	3.92±0.03
F6	97.40±0.85	98.21±0.52	3.96±0.03
F7	96.80±0.81	98.95±0.64	3.96±0.02
F8	98.14±0.66	98.95±0.38	3.93±0.04
F9	98.75±0.49	98.21±0.82	3.93±0.03

*All values are mean ± SD, (n=3)



Invitro Permeation Drug Release of formulations F1 to F9 Optimized Batches: F7

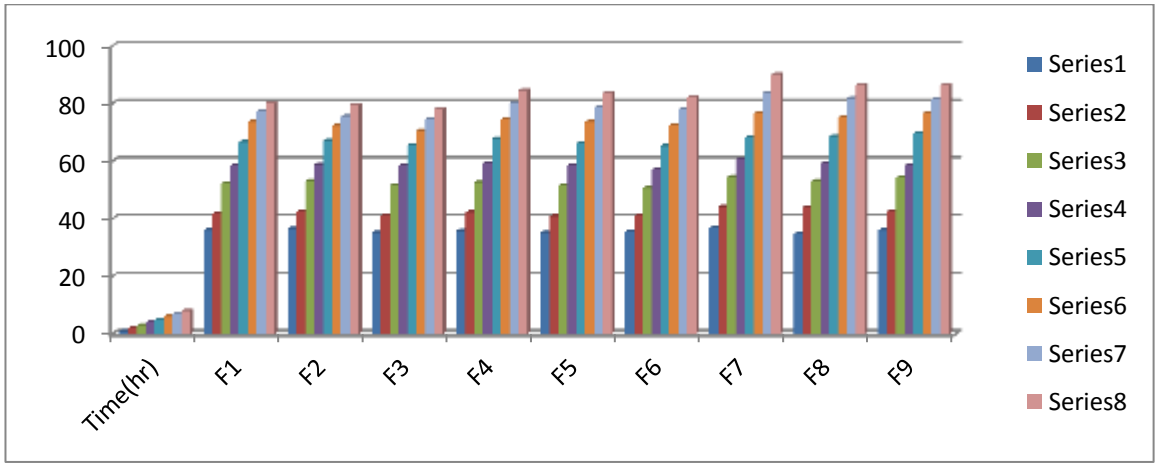


Fig no-10.11 Invitro Permeation Drug Release of formulations F1 to F9 (Rat Skin).

Optimized Batches: F7,

1. *In-Vitro* Drug Release:

Table No.10..23: *In-Vitro* % Drug Release of Optimized batches F7 .

Time (Hr)	% Drug Release	
	F7	
1	36.8	
2	48.6	
3	60.8	
4	71.6	
5	81.0	
6	86.4	
7	92.4	
8	96.6	

*All values are mean ± SD, (n=3)

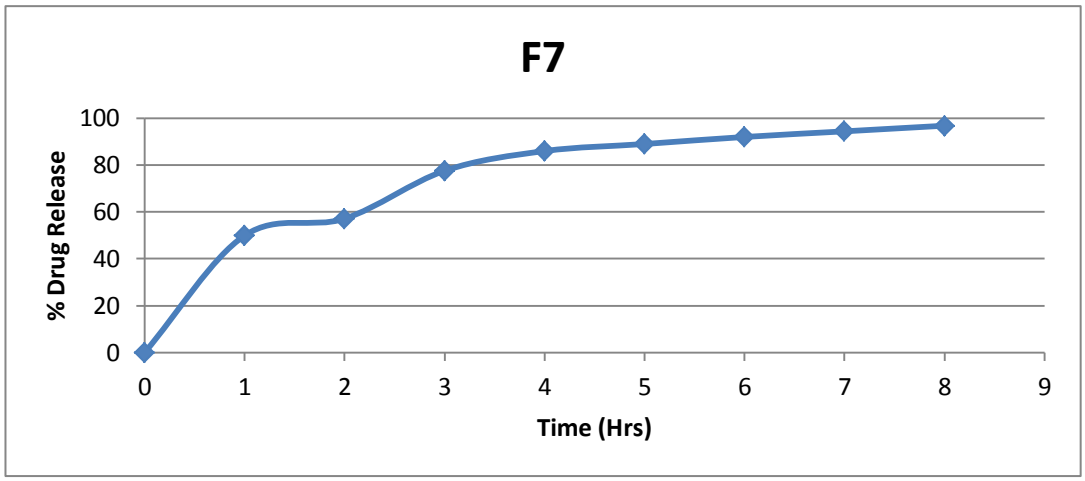


Fig no-10.23 graph of Optimized Batches F7 %Invitro Drug Release.

Conclusion:

- Patches of Ethyl cellulose, polyvinyl pyrrolidone propylene glycol showed the desired film forming characteristics.
- Effect polyvinyl pyrrolidone and Propylene glycol on cumulative drug release and Folding Endurance of patch was compared. Patch of formulation F7 showed higher drug release and higher Permeation and higher Invivo Absorption by (Rat Skin) than patches of other formulations and desired physical evaluation parameters.
- Hence, formulation F7 were taken for further comparative study. Patches of other formulation compare showed higher drug release and higher Invitro permeation higher, In-vivo Absorptoin than the patch of other formulation.
- So, the formulations F7 containing 3.0 gm of Ethyl Cellulose, 2.0gm polyvinyl pyrrolidoneand respectively and 5.0 ml of Propylene glycol were considered to be the optimized formulations.
- It was found that the increase in concentration of propylene glycol ,polyvinyl pyrrolidone in formulation shows sustained drug release and higher Invitro Permeation, higher % drug Release, higher Invivo absorption while increase in concentration of Propylene glycol, increases % drug release and Increases Folding Endurance.
- It can be concluded that the Transdermal Patch of Iodine can be formulated by using Ethyl Cellulose, polyvinyl pyrrolidone as a film forming polymer and Propylene glycol as a plasticizer and Penetration Enhancer.
- Finally it can be concluded that the Transdermal drug delivery of Iodine Patch can be achieved and prove that In-vivo Study And Skin Irritation Study, Invitro permeation, Invitro drug release, through a Transdermal patch formulated by using Ethyl Cellulose, Polyvinyl pyrrolidone and Propylene Glycol.

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