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Original Research Article

DESIGNING AND CHARACTERIZATION OF CHLORPHENERAMINE MALEATE TRANSDERMAL PATCHES

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ABSTRACT

Transdermal drug delivery system (TDDS) provides a means to sustain drug release as well as reduce the intensity of action and thus reduce the side effects associated with its oral therapy. In the present study an attempt was made to develop a suitable matrix type transdermal patch of Chlorpheniramine maleate with different ratios of polymeric systems of agar, acacia, polyvinyl alcohol, polyvinyl pyrolidine, Eudragit RS 100 by solvent evaporation technique by using glycerin and polyethylene glycol as plasticizer for improvement of bioavailability of drug. The physicochemical compatibility of the drug and the polymers studied by infrared spectroscopy suggested absence of any incompatibility. Formulated transdermal films were physically evaluated with regard to thickness, weight variation, drug content, flatness, tensile strength, folding endurance, percentage of moisture content and water vapour transmission rate. The in vitro release of the drug from the formulations was studied using goat skin as a semi permeable membrane and CM7 shown the maximum response. From the In vitro dissolution data showed that formulation CM7 showed better release of drug than the other polymers combinations. Hence CM7 is the best formulation among the various formulation used in this research work.

Key words: Polymers, Sustained release, Bioavailability.

INTRODUCTION:

The method by which a drug is delivered can have a significant effect on its efficacy. New strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bio-conjugate chemistry, and molecular biology. To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under development. Controlled drug release and subsequent biodegradation are important for developing successful formulations. Potential release mechanisms involve: (i) desorption of surface-bound /adsorbed drugs; (ii) diffusion through the carrier matrix; (iii) diffusion (in the case of nanocapsules) through the carrier wall; (iv) carrier matrix erosion; and (v) a combined erosion /diffusion process. A transdermal drug delivery device, which may be of an active or a passive design, is a device which provides an alternative route for administering medication. These devices allow for pharmaceuticals to be delivered across the skin barrier. Transdermal drug delivery systems are topically administered medicaments in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate. Through a diffusion process, the drug enters the bloodstream directly through the skin. Since there is high concentration on the patch and low concentration in the blood, the drug will keep diffusing into the blood for a long period of time, maintaining the constant concentration of drug in the blood flow. This approach to drug delivery offers many advantages over traditional methods. As a substitute for the oral route, transdermal drug delivery enables the avoidance of gastrointestinal absorption, with its associated pitfalls of enzymatic and pH associated deactivation. Chlorpheniramine maleate a histamine H1 antagonist used in allergic reactions, hay fever, rhinitis, urticaria, and asthma. They prevent, but do not reverse the responses mediated by histamine. CPM antagonizes most of the pharmacological effects of histamine, including urticaria and pruritus. Also, CPM, like other antihistamines, produces a drying effect on various mucosa's by preventing the responses to acetylcholine that are mediated via muscarinic receptors[1,2]. The CPM is a typical cationic amphiphillic amine drug (CAD); characterized by the hydrophobic ring structure of the molecule and the hydrophilic side chain with a charged cationic amino group. This above physiochemical property of CPM is similar to other CADs; therefore it was chosen as a model drug for the present study.

MATERIALS AND METHODOLOGY:

Chlorpheniramine Maleate is a gift sample obtained from Supriya life sciences, pvt ltd, Ratnagiri, India. Eudragit RS – 100 obtained from Glukem pharmaceuticals, pvt ltd, Hyderabad,

India. Agar, Polyvinyl Alcohol and polyvinyl pyrolidine were obtained from Loba chemie pvt., ltd., Mumbai, India. Acacia Molychem pvt., ltd.,Mumbai, India. All the other chemicals used in the study were of analytical grade.

Methodology:

The method which is involved in the preparation of Chlorpheniramine maleate sustain release transdermal patches.

The steps which are involved are as follows:

Weighing of drug, polymer and plasticizer

⇩

Dissolve plasticizer in sufficient quantity of water

⇩

To this solution sufficient quantity of polymer is added

⇩

This solution is heated with stirring at 90°C till the desired consistency is obtained

⇩

It is allowed to cooled when temperature reaches at 72°C then the drug is added

⇩

Drug containing solution was poured into the transdermal patch mould and kept in a hot air oven for overnight at 45°C.

Accurately weighed quantities of all ingredients (Drug, Glycerol, PEG, Agar, Acacia, PVA, PVP and Eudragit RS -100) were taken as per the table 1. In this formulation plasticizer is dissolved in sufficient quantity of water. To this solution polymer is added and heated with stirring at 90°C until the desired consistency is obtain. Then the solution is allowed to cooled when temperature reaches at 72°C then the drug is added, stirred till it dissolved. Then it was poured into transdermal patch mould and kept in a hot air oven for overnight at 45°C. The obtained patches were as shown in Fig.1.

Table.1.Development of different formulations containing, varying proportions of polymers

Formulation code	Drug (gm)	Glycerol (gm)	PEG (gm)	Agar (gm)	Acacia (gm)	PVA (gm)	PVP (gm)	Eudragit RS100(mg)	Water (ml)
CM 1	0.5	7.5	-	0.75	-	-	-	-	Qs
CM 2	0.5	7.5	-	-	0.75	-	-	-	Qs
CM 3	0.5	7.5	-	0.625	0.125	-	-	-	Qs
CM 4	0.5	-	3.75	-	-	2.5	2.5	-	Qs
CM 5	0.5	-	3.75	-	-	3	2	-	Qs
CM 6	0.5	-	3.50	-	-	3.5	1.5	-	Qs
CM 7	0.5	7.5	-	0.625	-	-	-	0.125	Qs

Fig.1.Preparation of transdermal patches in the modified mould and obtained patches

EVALUATION:

Thickness:

By using Vernier calipers at three different places the thickness of the patches was measured and the average was calculated.[3]

Uniformity of weight:

Weight variation is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not deviate significantly from the average weight.[4]

Folding endurance:

In this patch is folded as number of times at same place till breaks. The number of times till the film could be folded at the same place without breaking gives the value of folding endurance.[5]

Tensile strength and percentage Elongation:

In tensile strength determination maximum stress is applied at same point till the patch breaks. Percentage elongation is measured by capacity of patch to deform till it breaks. Rectangular patch strips of 25.4mm X 50mm were fixed between the jaws of the instrument. The load on the strip was gradually increased to a maximum at a speed of 50mm / min and the change in the length of the strips that occurred with increasing stress was measured. Tensile strength and percent elongation of three patches of each batch were measured.[6]

Percentage Moisture content:

The prepared films were weighed individually and kept them in a

desiccators containing fused calcium chloride at room temperature for 24 hrs. After 24hrs the films were reweighed and percentage moisture content were determine from the below mentioned formula. [7, 8, 9]

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

Percentage Moisture uptake:

The prepared films were weighed individually and kept them in a desiccators containing saturated solution of potassium chloride in order to maintain 84% RH. After 24hrs the films were reweighed and the percentage moisture uptake was determined from the below mentioned formula. [7, 8, 9]

$$\% \text{ Moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Water vapour permeability: Glass vials of 5 ml capacity were thoroughly washed and dried to a constant weight in an oven. 1gm of fused Calcium chloride was taken in the vials & the polymer films were fixed over the brim with the help of an adhesive tape. Then initial weight of the vial is determined and stored in a humidity chamber at 85 % RH condition for a period of 24 hours. The polymer films were removed and their final weight is recorded. [10]

Drug content: A specified area of patch was dissolved in a suitable solvent in specific volume. Then the solution is filtered and amount of drug present is analyzed with the help of UV. [9, 10]

In vitro drug dissolution studies: Drug release mechanisms and kinetics are two characteristics of the dosage forms which play an important role in describing the drug dissolution profile from controlled release dosage forms and hence their in vivo performance. The dissolution data is fitted to these models and the best fit is obtained to describe the release mechanism of the drug.

- There are various methods available for determination of drug release rate of TDDS The Paddle over Disc(USP apparatus 5/ Ph Eur 2.9.4.1):
- This method is identical to USP paddle dissolution apparatus, except that the transdermal system is attached to a disc or cell resting at the bottom of the vessel which contains medium at 32 ±5°C.
- The Cylinder modified USP Basket (USP apparatus 6 / PhEur 2.9.4.3).
- This method is similar to the USP basket type dissolution apparatus, except that the system is attached to the surface of a hollow cylinder immersed in medium at 32±5°C. [11]

In- vitro permeation studies: The diffusion studies were done to get an idea

of permeation of drug through barrier from the transdermal system. In vitro studies are also done for TDDS development. Usually, two types of diffusion cells are used as horizontal and vertical. The Franz and Keshary Chien (K-C) type of diffusion cells are of horizontal type of cells. In this work, K-C type of diffusion cell was used. Diffusion cells generally comprise two compartments, one containing the active component (donor compartment) and the other containing receptor solution (receptor compartment), separated by barrier i.e. albino rate abdominal skin. The cell consisted of sampling port and temperature maintaining jacket. The outlet and inlet was connected with latex tube so the jacket had stagnant water inside and heat was provided by hot plate. The stainless steel pin was used to stir the receptor solution using magnetic stirrer. The goat abdominal skin was placed on receptor compartment and both compartments held tight by clamps. Phosphate buffer pH 7.4 was used as receptor solution. The volume of diffusion cell was 15 ml and stirred with bent stainless steel pin. The temperature was maintained at 37 ± 2°C with the help of magnetic stirrer. The diffusion was carried out for 24 hours and 1 ml sample was withdrawn at an interval of 1, 2, 3, 4, 5, 6, 7, 8, 10, 12 and 24 hour. The same volume of phosphate buffer pH 7.4 was added to receptor compartment to maintain sink conditions and the samples were analyzed at 220nm in UV spectrophotometer. [7, 8]

Fourier Transform- Infrared Spectroscopic Analysis (FT-IR): Drug polymer interactions were studied by FT-IR spectroscopy. 2mg of pure drug, and excipients alone and drug: excipients (1:1) samples were prepared and properly mixed with potassium bromide to form a uniform mixture. By applying pressure small quantity of the powder was compressed into a thin semitransparent pellet. The IR-spectrum of the pellet from 450- 4000cm^{-1} was recorded taking air as the reference and compared to study any interference.[12]

Drug release kinetics: Model dependent methods are based on different mathematical functions, which describe the dissolution profile. Once a suitable function has been selected, the dissolution profiles are evaluated depending on the derived model parameters. The model dependent approaches included zero order, first order, Higuchi, Hixson-Crowell, Korsmeyer-Peppas, Baker-Lonsdale, Weibull, Hopfenberg, Gompertz and regression models. [13, 14]

Zero Order Model: Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation:

$$Q_0 \text{ n } Qt = K_0 t$$

Rearrangement of above equation yields:

$$Q_t = Q_0 + K_0 t$$

Where,

Qt is the amount of drug dissolved in time *t,*

Q_0 is the initial amount of drug in the solution (most times, $Q_0 = 0$) and

K_0 is the zero order release constant, expressed in units of concentration/time.

To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as cumulative amount of drug released *versus* time. [15, 16]

First Order Model: This model has also been used to describe absorption and/or elimination of some although it is difficult to conceptualize this mechanism on a theoretical basis. The release of the drug which followed first order kinetics can be expressed by the equation:

$$dc / dt = -Kc$$

Where,

K is first order rate constant expressed in units of time-1.

The above Equation can be expressed as:

$$\log C = \log C_0 - Kt / 2.303$$

where,

C_0 is the initial concentration of drug,

k is the first order rate constant, and

t is the time.

The data obtained are plotted as log cumulative percentage of drug remaining *vs.* time which would yield a straight line with a slope of -K/2.303.

Application: This relationship can be used to describe the drug dissolution in pharmaceutical dosage forms such as those containing water-soluble drugs in porous matrices. [17, 18]

Higuchi Model: A form of the Higuchi Square Root Law is given by equation:

$$Q = K_s \sqrt{t}$$

Where

Q = Amount of drug dissolved at time t

K_s = Higuchi rate constant

The Higuchi square root equation describes the release from systems where the solid drug is dispersed in an insoluble matrix, and the rate of drug release is related to the rate of drug diffusion.[19, 20, 21]

Korsmeyer and Peppas Release Model:

The release rate data were fitted to the following equation,

$$M_t / M_\infty = K.t^n$$

Where

M_t / M_∞ is the fraction of drug released,

'K' is the release constant,'t' is the release time.

'n' is diffusion exponent, if n is equal to 0.89, the release is zero order.

In this model, the value of *n* characterizes the release mechanism of drug. For the case of cylindrical tablets, $0.45 \leq n$ corresponds to a Fickian diffusion mechanism, $0.45 < n < 0.89$ to non-Fickian transport, n = 0.89 to Case II (relaxational) transport, and $n > 0.89$ to super case II transport.[22, 24] To find out the exponent of *n* the portion of the release curve, where $Mt / M\infty < 0.6$ should only be used. To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as log cumulative percentage drug release *versus* log time.

Hixson Model: This model applies to pharmaceutical dosage form such as tablets, where the dissolution occurs in planes that are parallel to the drug surface. To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as cube root of drug percentage remaining in matrix *versus* time.

$$Q_0^{1/3} - Q_1^{1/3} = Ks\ t$$

Where,

Ks-constant incorporating the surface volume relation

Q0-initial amount of drug in the solution

Q1-amount of drug dissolved in time t.

RESULTS:

Physicochemical evaluation:

All the prepared formulations were subjected to physicochemical evaluation and the results were depicted in the table 2.

Table.2.Physicochemical Parameters of Formulated Patches

Formulation code	Weight uniformity (mg)	Thickness (mm)	Flatness (%)
CM1	0.26	0.2	0% Constriction
CM2	0.25	0.5	0% Constriction
CM3	0.10	0.5	0% Constriction
CM4	0.13	0.4	0% Constriction
CM5	0.19	0.2	0% Constriction
CM6	011	0.3	0% Constriction
CM7	0.42	0.7	0% Constriction

Folding Endurance and Tensile Strength data: All the seven formulated matrix patches were subjected to folding endurance test and tensile strength was measured by using modified apparatus using pan and weights and the results were given in table 3.

Table.3.Folding Endurance and Tensile Strength of all formulations

Formulation code	Folding insurance (times)	Tensile strength (kg / m^2)
CM1	18	21
CM2	12	19
CM3	29	23
CM4	>500	25
CM5	>600	20
CM6	210	19
CM7	14	21

Percentage moisture loss and moisture absorption, water vapour transmission data:

Percentage moisture loss, moisture absorption and water vapour transmission test were performed by placing the specified area of the prepared patches in desiccators containing fused calcium chloride and saturated potassium chloride respectively. And the results were as shown in table 4.

Table.4. Moisture Loss, Moisture Absorption and Water Vapour Transmission Rate data of all formulations

Formulation code	Moisture loss (%)	Moisture absorption (%)	Water vapour transmission
CM1	21	4.3	0.02
CM2	46.6	21.7	0.044
CM3	38.4	7.14	0.063
CM4	13.3	5	0.031
CM5	35.7	5.5	0.017
CM6	31.2	6.25	0.030
CM7	20.05	6.4	0.044

Drug content uniformity: All the formulated patches were subjected to drug content and the results were depicted as table 5.

Table.5.Drug content uniformity

Formulation code	Drug content uniformity (%)
CM1	87.5
CM2	89.15
CM3	90.15
CM4	92.42
CM5	88.56
CM6	89.35
CM7	94.65

In vitro dissolution data:

In vitro drug release study was performed for all the formulations using modified USP apparatus 5 using pH 7.4 phosphate buffer solution maintained at 37 ± 0.5^{0}C. The test was performed for 8 hrs for all the preparations and the results were given in the table 6 and graphically given in Fig.2.

Table.6.Comparison of dissolution profiles of all formulated patches

Time (hrs)	% Drug release						
	CM1	CM2	CM3	CM4	CM5	CM6	CM7
1	34.533	35.182	36.262	29.130	21.566	21.566	46.204
2	35.157	38.403	40.354	30.805	23.414	23.414	55.322
3	36.000	41.425	41.441	32.488	24.841	24.841	60.815
4	37.495	44.246	42.534	34.395	25.193	25.193	62.879
5	43.103	45.353	48.602	43.445	28.789	28.789	66.249
6	44.635	47.113	54.486	46.708	30.459	30.459	67.907
7	45.525	48.449	58.025	50.421	32.137	32.137	70.436
8	49.445	53.033	60.716	53.071	32.960	32.960	73.194

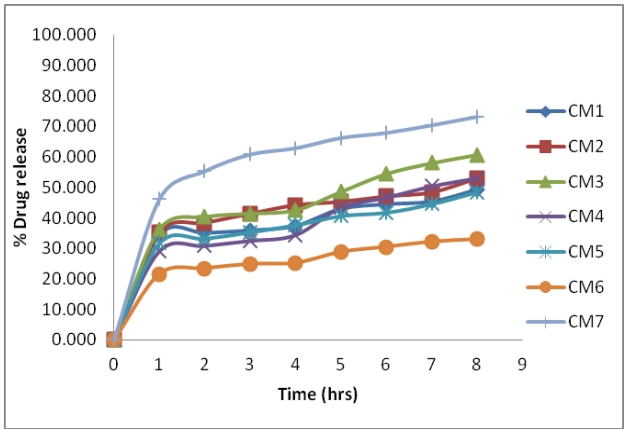

Fig.2. Comparison of dissolution profiles of all formulated patches

In vitro permeation studies:

In vitro permeation was done by using excised sheep abdomen skin and the formulated patches were subjected to permeation study and the study was continued up to 8 hrs and the results were tabulated in the table 7 and the images of permeation test was displayed in Fig.3 and the obtained data was graphically depicted in Fig.4.

Fig.3. Images for In –vitro permeation study

Table.7.Comparison of in- vitro permeation data of all formulated patches

Time (hrs)	% In – Vitro Permeation						
	CM1	CM2	CM3	CM4	CM5	CM6	CM7
1	22.327	27.666	23.758	35.228	11.892	6.948	11.694
2	25.147	28.516	24.233	40.975	17.370	8.768	20.036
3	25.937	29.372	27.872	45.736	20.086	9.435	26.958
4	27.030	31.717	29.795	46.719	21.663	10.705	33.813
5	28.136	33.208	31.152	48.100	22.373	11.008	36.048
6	29.846	36.496	32.327	49.392	22.991	11.313	37.821
7	30.393	38.355	33.415	50.791	23.612	11.818	38.626
8	31.830	41.127	35.898	52.693	24.139	12.131	39.434

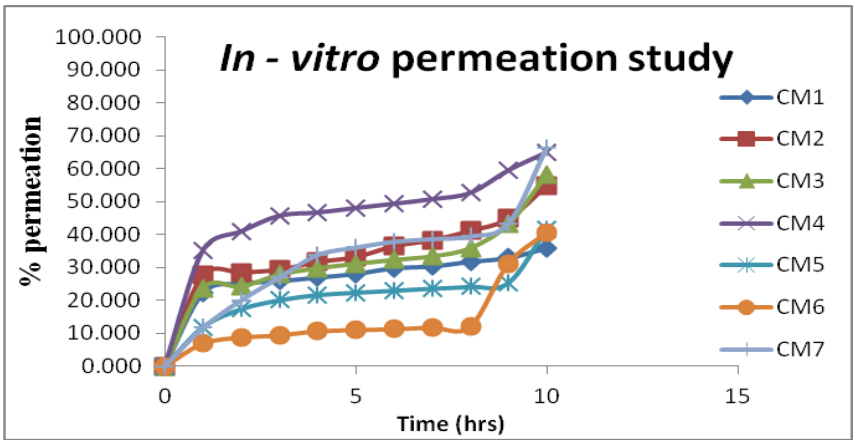

Fig.4.Comparison of in- vitro permeation plot of all formulated patches

Fourier Transform- Infrared Spectroscopic Analysis (FT-IR):

FT – IR studies were performed to study out drug and excipients compatibility. Alone drug, polymers and combination of all each polymer with drug (1:1), and also the selected best formulation of all the formulated patches were subjected for the study. And the results were given in Fig.5-11.

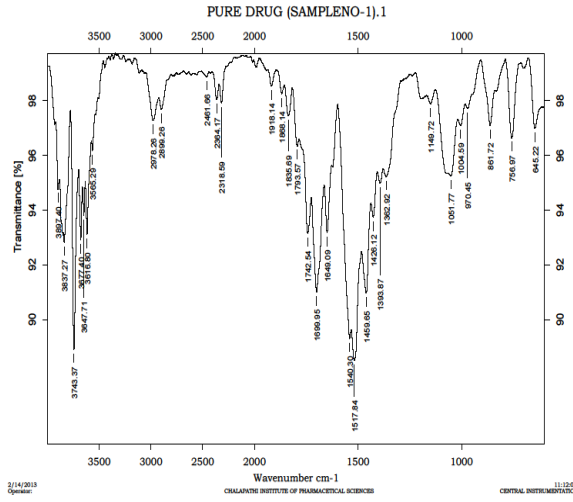

Fig.5.FT-IR spectra of pure drug

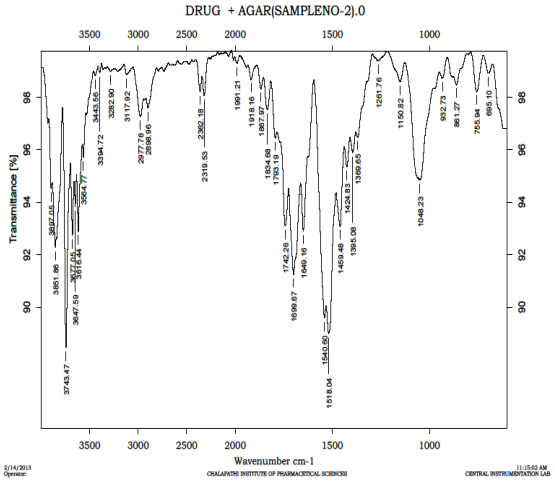

Fig.6.FT-IR spectra of pure drug and agar

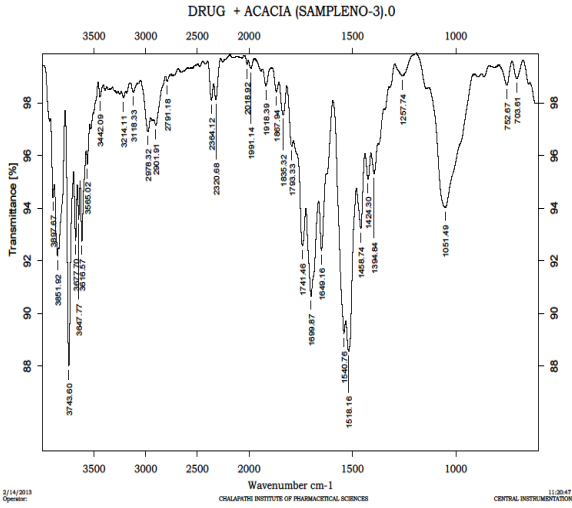

Fig.7. FT-IR spectra of pure drug and acacia

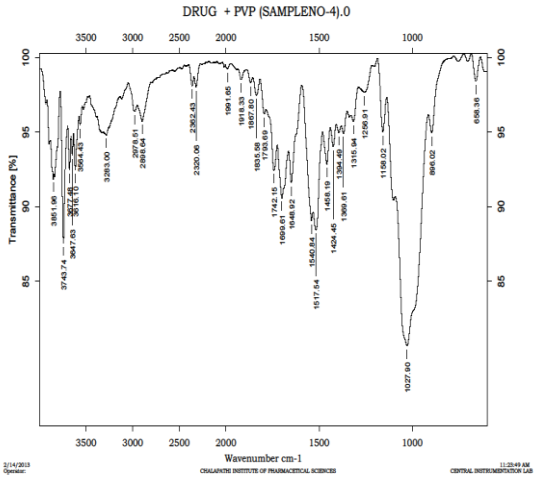

Fig.8.FT-IR spectra of pure drug and PVP

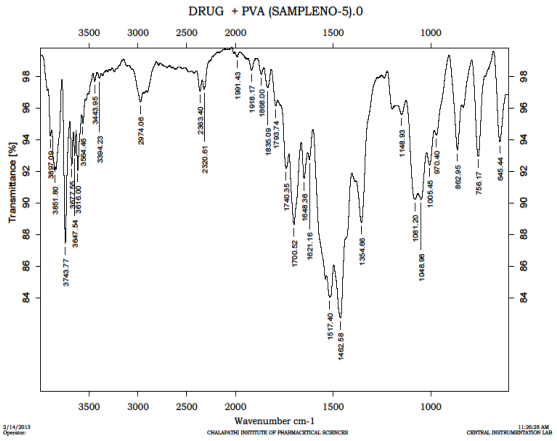

Fig.9.FT-IR spectra of pure drug and PVA

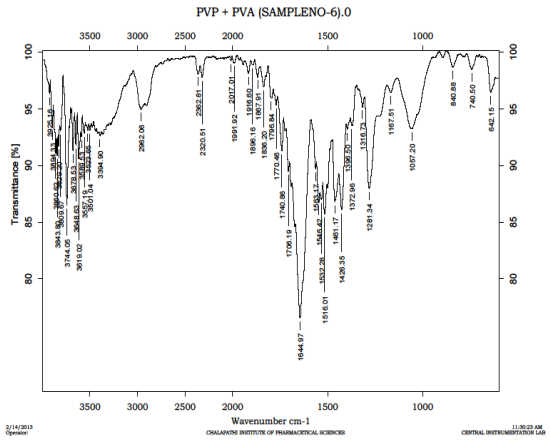

Fig.10.FT-IR spectra of pure drug and PVA + PVP

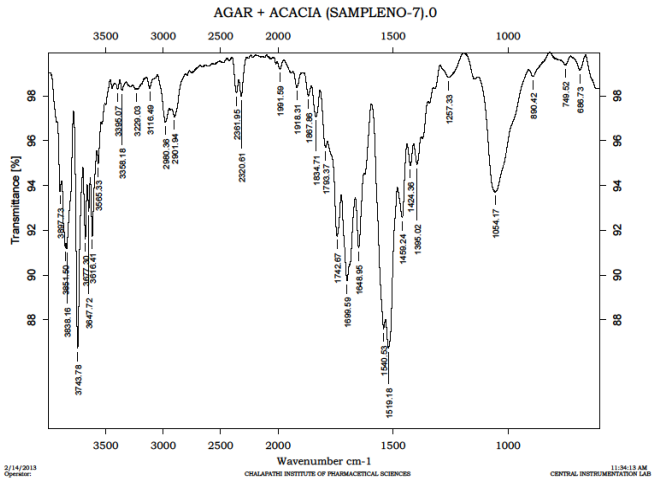

Fig.11.FT-IR spectra of pure drug and Agar + Acacia

Drug release kinetics:

The release kinetics was performed of all the formulation using obtained dissolution data. And the results were shown in table 8.

Table.8.Data showing drug release kinetics for all the prepared formulations

Formulation code	Zero order	First order	Matrix	Korsmeyer			Hixson
	R	R	R	R	n	k	R
CM1	0.2817	0.5672	0.8862	0.9003	0.1758	32.0028	0.4908
CM2	0.1949	0.5455	0.8875	0.9816	0.1841	34.3320	0.4587
CM3	0.6046	0.8191	0.9433	0.9309	0.2497	33.7989	0.7603
CM4	0.7485	0.8770	0.9677	0.9201	0.3107	25.8895	0.8411
CM5	0.3917	0.6241	0.9077	0.9494	0.1987	29.8318	0.5581
CM6	0.4364	0.5798	0.9172	0.9554	0.2124	20.4733	0.5365
CM7	0.2781	0.7191	0.9020	0.9956	0.2115	47.0601	0.6114

DISCUSSION:

All the formulations were subjected to Weight uniformity test and the values ranges between 0.10 to 0.42 (mg). It was observed that the formulation CM7 exhibits more uniformity in weight compare to all formulations. Thickness was performed by using Vernier calipers for all the formulations at different positions. Thickness values ranging from 0.2 to 0.7 mm. the formulation CM7 exhibits more thickness this was due to the fact that Eudragit L 100 is more viscous than other polymers. Flatness was calculated by measuring length of the patches at middle, right and left side portions, so it was observed that there was no constriction in the prepared patches. Folding endurance of formulation CM5 is more indicating that the patch is more mechanically stable. Agar and acacia containing formulations are able to brittle easily and was observed in CM1, CM2, CM3 and CM7. Tensile strength of patches ranges from 19 to 25 (kg/m^2). The formulation CM4 was observed that it was able to withstand for high pressure. Percentage Moisture Loss test was performed for all the formulation it indicates that the formulation CM2 lost more amount of water from patch. Percentage moisture Percentage moisture absorption study was conducted for all the prepared formulations. Moisture loss and moisture absorption values ranges from13.3 to 38.4 and 5 to 21.7% respectively. Results concluded that CM2 formulation attains more amount of moisture absorption and more amount of moisture to be loss on storage. All the formulations were subjected to water vapour evaporation test results revealed that all the formulations are within the I.P specified limits.

All the prepared patches were subjected for in -vitro dissolution studies. The percentage drug release values ranges from 49.445 – 73.19%. Formulations CM5 and CM6 were found to give very slow drug

release compare to other formulations due to the presence of combination of two polymers PVA and PVP in varying proportions. Results showed that out of seven formulations, the transdermal patches prepared with eudragit L-100 as polymer has good drug release profile of 73.19% for 8hrs (CM7) when compared to other formulations containing varying proportions of agar, accacia, PVP and PVA. This was due to the fact that by increasing the density of polymer matrix at high concentration results in an increase in diffusional path length.This may finally decrease the drug release from polymer matrix and it was found to be that the drug release from theformulation CM7 is with in the specified limits according to USP. (i.e., near to 80% with in 8 hrs). Thus it was concluded that formulation CM7 was selected as the best formulation compare to all the prepared formulations. Finally it was concluded that all the hydrophyllic co-polymers which were used for the study provides the sustained release of chlorpheneramine maleate as per the limits according to the USP. In vitro permeation was performed by using sheep skin using pH 7.8 phosphate buffer solution. Percentage permeation values ranges from 12.31 to 52.693%. Formulation CM4 had more permeability where as formulation CM6 exhibits less permeability due to presence of various polymeric material properties. All the prepared patches exhibits good rate of permeation in presence of pH 7.8 and provides good permeation rate over a prolonged period of 8hrs. A comparison of the FT-IR spectrums of the individual polymers /drug like Eudragit RS 100, Agar, Acacia, PVP and PVA and also best formulation matrix patch was carried out to observe any spectral shifts in the matrix. The FTIR spectra of the optimized formulations pure drug: Eudragit RS 100: Agar [Scanned 1cm^2 patch containing 585µgm] revealed all the peaks of the polymers was obtained in the spectra. The characteristics of Eudragit RS 100 and Agar peaks were observed at 3743.51cm^{-1} and 1742.67cm^{-1}, 1540.68cm^{-1}, 1459.31cm^{-1}, 1063.45cm^{-1} and 752.03cm^{-1} respectively. Results concluded that there were no significant shifts in the peaks corresponding to the drug or polymers were observed in the formulation matrix. Some characteristic peaks corresponding to the drug were found to be overlapping in the region as that of the polymer. From the data of drug release, it was found that, all the formulations follow matrix and korsmeyer- peppas model. The Higuchi matrix equation describes the release from systems where the solid drug is dispersed in an insoluble matrix, and the rate of drug release is related to the rate of drug diffusion**.** The n value obtained for all the formulations is < 0.25 **(**0.45 ≤ n) concluded that the prepared patches follows Fickian diffusion mechanism of drug transport.

CONCLUSION:

Our main aim is to develop a suitable matrix type transdermal patch of Chlorpheniramine maleate with different ratios of polymeric systems of agar, acacia, polyvinyl alcohol, polyvinyl pyrolidine, Eudragit RS 100 by the solvent evaporation technique. Different formulations were prepared using 2mg of

drug.The physicochemical compatibility of the drug and the polymers studied by infrared spectroscopy suggested absence of any incompatibility. Formulated transdermal films were physically evaluated with regard to thickness, weight variation, drug content, flatness, tensile strength, folding endurance, percentage of moisture content and water vapour transmission rate and found to be under specified limits. Because use of Agar and Acacia in some of the above formulation we get gel type patches and they readily melt at body temperature and easily drug release take place but their folding endurance is very less compared to PVA and PVP polymers used in other formulations. From the above drug release data it was observed that formulation CM7 is proved to be best among the prepared formulations which may be used for prolong drug release for more than 8 hrs, thereby improving patient compliance and bioavailability.

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