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Formulation and Evaluation of Haloperidol Decanoate Containing Transdermal Patch for the Treatment of Psychosis

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ABSTRACT

Transdermal patches are a non-invasive method of drug administration. It is an adhesive patch designed to deliver a specific dose of medication through the skin and into the bloodstream throughout the body. Transdermal drug delivery has several advantages over other routes of administration, for instance, it is less invasive, patient-friendly, and has the ability to bypass first-pass metabolism and the destructive acidic environment of the stomach that occurs upon the oral ingestion of drugs. For decades, transdermal patches have attracted attention and were used to deliver drugs such as nicotine, fentanyl, nitroglycerin, and clonidine to treat various diseases or conditions. Recently, this method is also being explored as a means of delivering biologics in various applications. The most common routes of drug delivery are the oral and parenteral routes with the majority of small molecule drugs conventionally delivered orally. The oral route has the advantage of pre-determined doses, portability and patient self-administration. For these reasons, the oral route remains the most convenient means of delivering medications

Keyword: *Transdermal drug delivery system, Patch, Film, haloperidol decanoate, Natural polymer*.

1. INTRODUCTION

Transdermal patches can be tailored and developed according to the physicochemical properties of active and inactive components, and applicability for long-term use. Transdermal route of drug delivery can achieve local and systemic therapeutic effects. Transdermal drug delivery is an attractive substitute for oral drug administration as it bypasses first pass metabolism, gastrointestinal effects and, moreover, it can overcome the poor patient compliance associated with other drug delivery routes [1]. Transdermal drug delivery is self-administered, allowing the drug to pass through intact skin over a controlled period of time to achieve a local or systemic effect. Drugs can be delivered through transdermal patches in dissolved lipid based form enabling them to produce the required efficacy [2]. Transdermal patches are attractive as they are noninvasive, easy to use, and can also deliver multiple doses for an extended time period, while also showing patient compliance and cost-effectiveness. The approach to transdermal patches may either be matrix or reservoir approach polymeric systems that house the drug such that it diffuses through the polymer by the way of skin beneath for reaching the systemic circulation in a controlled manner [3]. A transdermal patch is an interesting approach for breast cancer since it can act as a reservoir for the drug at the required site. On an animal observation basis, the transdermal patch of anastrazole gave high anastrazole accumulation in the area beneath the patch application site compared to oral administration [4]. The application of transdermal patches is not just limited to direct treatment or prevention but may also show some significance indirectly. Transdermal patches are adhesive patches placed on the skin to deliver a specific dose of a drug through the skin into the bloodstream [5]. The primary objective of drug delivery through this dosage form is the localized release of drugs to enhance their presence and absorption at the desired site, which can be referred to as a drug release control system. Painless application, less frequent replacement, and greater dosing flexibility have led to the research and development of transdermal patches for the treatment of skin wounds. Biopolymers have been extensively studied for the manufacture of transdermal patches due to their safety, biocompatibility, low toxicity, and controlled degradation by human enzymes [6]. A transdermal patch consists of an adhesive patch incorporating a drug which is either evenly distributed within the

adhesive layer, in a matrix with a full or peripheral adhesive layer or as a reservoir with a rate controlling membrane and full or peripheral adhesive layer. Transdermal patches are a type of drug delivery systems that are used to introduce medications through the

skin for curative purposes and to replace other drug delivery systems. For many centuries, people have used different materials to treat various skin diseases [7]. Nowadays, a wide range of topical products has been introduced to achieve therapeutic effects. Transdermal patches are attractive as they are noninvasive, easy to use, and can also deliver multiple doses for an extended time period, while also showing patient compliance and cost-effectiveness [8]. The approach to transdermal patches may either be matrix or reservoir approach polymeric systems that house the drug such that it diffuses through the polymer by the way of skin beneath for reaching the systemic circulation in a controlled manner. The most relevant dosage form for transdermal drug delivery is the transdermal patch, an adhesive flexible preparation that firmly sticks to the unbroken skin to constantly deliver an amount of drug through the skin layers. An outer layer, impermeable to the drug and normally impermeable to water, supports and protects the preparation [9]. Transdermal patches are deliberately designed to deliver predictable and pharmaceutically significant doses of selected drugs. In the context of this chapter they are primarily of interest in that they illustrate some properties of compounds that are conducive to dermal absorption. Only a limited subset of pharmaceuticals can be practicably delivered via transdermal patches [10]. The conventional routes of medication delivery have many inherent limitations which could potentially be overcome by advanced drug delivery methodologies such as transdermal drug delivery (TDD). We may be improving the therapeutic effect of drugs via approaches as transdermal patch hold on to part of skin. The power of adhesion of patch creates good penetration ability of TDDs by using arrangement of different penetration enhancers. The aim of proposed work is to develop a polymeric transdermal patch for haloperidol an antipsychotic drug for controlled released for maintenance therapy

2. MATERIAL AND METHODS

Identification of maximum absorption wavelength (λmax): The identification of absorption maxima was determined by UV scanning of drug solution under ultraviolet spectrophotometer between 200 to 400 nm wavelengths offer drug sample i.e. haloperidol.

Preparation of standard calibration curve: Accurately weighed required quantity 50 mg of drug sample i.e. haloperidol mixed in volumetric flask containing 50 ml of phosphate buffer pH 7.4 solvent. The concentration of resulting solutions were 10 µg / ml, 20 µg / ml, 30 µg / ml, upto 50 µg / ml respectively. The absorbance of all resulting solution was calculated individually at 221 nm with phosphate buffer pH 7.4 as a blank. The absorbance was measured and standard curve was plotted between absorbance vs. concentration.

Validation of analytical method development

Specificity test: The specificity test for the analytical method is defined as the capability to notice the analyte of attention in the occurrence of interfering material. Specificity is exposed by spiking recognized stage of impurities or corrupting agents in to a test with a known quantity of the analyte of concentration.

Precision test: As per the ICH guidelines precision test was classified in to two parameters i.e.; repeatability test and intermediate precision test.

Repeatability test: The absorbance was determined at 221 nm for haloperidol using UV spectrophotometer. As per the guideline the percent RSD should not be more than 1 %.

Intermediate precision test: As per guidelines Intermediate precision test was also classified in to two parameters i.e.; Intra-day precision test and Inter-day precision precision test. Intra-day precision was determined at predetermined time interval within a day by assessment of the absorbance of 10 µg / ml drug haloperidol in phosphate buffer pH 7.4 solution. Inter-day precision test was determined on three different days by by assessment of the absorbance of 10 µg / ml drug haloperidol in phosphate buffer pH 7.4 solution. The absorbance was determined at 221 nm for haloperidol using UV spectrophotometer. As per the guideline the percent RSD should not be more than 1 %. The results of intra-day and inter-day precision test.

Accuracy test: The test of accuracy study of analytical method was specified as the difference between the measured quantity and the used quantity [11].

Preformulation Studies: The class of studies which need to be successfully completed before actually the formulation development and optimization starts are termed as preformulation studies. These studies are important as the processes for optimizing the delivery of candidate drug through determination of physicochemical properties of drug that could influence drug performance and development of an efficacious, safe and stable dosage form, These studies must resolve problems with drug analysis, stability, and pharmaceutical technology. Complete preformulation studies can decrease problems with instability of drug formulations during the shelf-life period caused by the selection of unsuitable excipients. The major parameters studied in this category are: characterization of the Active pharmaceutical ingredient (API), development of analytical methods, stability and compatibility studies of the drug with the excipients etc, It is through the proper completion of these preformulation studies that an optimal dosage form for desired therapeutic efficacy and utility could be designed. Preformulation studies of haloperidol were carried out, which included physicochemical characterization of drug (melting point, solubility, infra-red spectroscopy, particle size analysis, nuclear magnetic

resonance spectroscopy, X-ray diffraction studies and differential scanning calorimetry). Analytical procedure was developed for estimation of the drug in microspheres and solvent system.

Determination of sensory examination*:* The organoleptic properties of drug such as color, odor and taste will be noted visually.

Determination of microscopic examination: The microscopic examination of the drug sample was done to identify the nature / texture of the powder. The required amount of powder will spread on a glass slide and examine under phase contrast microscope [12].

Determination of physical characteristics*:*

Bulk Density: The drug powder was weighed accurately and kept through a glass funnel into graduated cylinder. The bulk density of a powder is the ratio of the mass of an untapped powder sample and its volume including the contribution of the interparticulate void volume. Hence, the bulk density depends on both the density of powder particles and the spatial arrangement of particles in the powder bed. The bulk density is expressed in grams per milliliter (g/mL) although the international unit is kilogram per cubic meter (1 g/mL = 1000 kg/m3) because the measurements are made using cylinders. It may also be expressed in grams per cubic centimeter (g/cm3). The bulking properties of a powder are dependent upon the preparation, treatment and storage of the sample, i.e. how it was handled. The particles can be packed to have a range of bulk densities and, moreover, the slightest disturbance of the powder bed may result in a changed bulk density. Thus, the bulk density of a powder is often very difficult to measure with good reproducibility and, in reporting the results, it is essential to specify how the determination was made. The bulk density of a powder is determined by measuring the volume of a known mass of powder sample that may have been passed through a sieve into a graduated cylinder.

Pass a quantity of powder sufficient to complete the test through a sieve with apertures greater than or equal to 1.0 mm, if necessary, to break up agglomerates that may have formed during storage; this must be done gently to avoid changing the nature of the material. Into a dry graduated cylinder of 250 mL (readable to 2 mL), gently introduce, without compacting, approximately 100 g of the test sample (m) weighed with 0.1 per cent accuracy. Carefully level the powder without compacting, if necessary, and read the unsettled apparent volume (V0) to the nearest graduated unit. Calculate the bulk density in g per mL by the formula m/V0. Generally, replicate determinations are desirable for the determination of this property.

Tapped density: The tapped density is an increased bulk density attained after mechanically tapping a container containing the powder sample. The tapped density is obtained by mechanically tapping a graduated measuring cylinder or vessel containing the powder sample. After observing the initial powder volume or mass, the measuring cylinder or vessel is mechanically tapped, and volume or mass readings are taken until little further volume or mass change is observed. The mechanical tapping is achieved by raising the cylinder or vessel and allowing it to drop, under its own mass, a specified distance by lifted 100 times by the use of a suitable tapped density tester.

Determination of flow properties: The flow properties of drug powder were characterized for identification of flow character of powder in terms of carr's index, hausner's ratio and angle of repose. The Carr's index ((I_C)) and Hausner's ratio (H_R) of drug powders will calculate according to following equation:

- Carr's Index (I_C) = $\rho_{Tapped} - \rho_{Bulk} / \rho_{Tapped}$
- Hausner's ratio (H_R) = $\rho_{Tapped} / \rho_{Bulk}$

The angle of repose (θ) was measured by fixed height method. This will calculate by following equation:

- Angle of repose (θ) = $\tan^{-1} 2\ H / D$

Where H is the surface area of the free standing height of the powder pile and D is diameter of pile that formed after powder flow from the glass funnel.

Determination of particle size distribution: Particle size distribution affects various physicochemical properties of the drug substances. The effect is not only limited to physical properties of solid drugs but also in some cases on their biopharmaceutical behavior. The mean diameter and particle size distribution of stavudine was determined by the Laser diffractometry using Malvern mastersizer 2000 through dry method. The dry sample of the drug was kept in the sample holder and measured for the particle size of the same.

Solubility determination: Saturation solubility of drug API (Haloperidol) was determined by incremental method analysis method in various solvents. The exact quantity of drug 50 mg was placed on the conical flask and the various solvents i.e. distilled water, 0.1 N HCl, Phosphate buffer pH 6.8 and pH 7.4 phosphate buffers separately filled in burette. The solvent was slowly added into drug containing conical flask until the drug was solubilized and stirred constantly overnight at 37±0.5ºC. The samples were filtered by using Whatmann filter paper (0.45µm pore size). The solubility assessment of drug was determined by calculation of concentration µg/ml unit.

Partition coefficient: The partition coefficient of drug samples was observed in mixed solvent of 100 ml containing n-

octanol: phosphate buffer pH 1,2. 100 mg of drug was added into 50 ml each of an n-octanol and buffer phase in a separating funnel. The mixture was shaken for 24 h until equilibrium reached. Both medium were divided and collected individually, filtered. The quantity of API dissolved in aqueous medium was diluted and determined by UV spectrophotometric method. The partition coefficient of API was calculated from the proportion between the concentrations of drug in organic and buffer solution quantity using following equation.

$\text{Log P}_{(\text{oct / pH 7.4})} = \text{Log } (C_{\text{noct}} - C_{\text{pH1.2}})$ equilibrium

Melting point: The melting point of drug samples were obtained by pinch of drug material sample filled in capillary tube by manually. Capillary tube sealed from one end with a bunsen flame burner individually. The filled capillary tube was kept in melting point apparatus and identified the temperature at which the drug was starting to melt.

Drug excipient compatibility study by Infrared spectroscopy of drugs: The functional group determination of drug samples was identified by IR spectroscopy. Infra-red spectroscopy was carried out by using Shimadzu IR Spectra photometer as method given below. The characteristic peaks were reported as wave number. The FTIR spectra of dried drug samples (Haloperidol) independently were obtain by FTIR spectrophotometer by means of the potassium bromide disc method. The drug sample was pulverized and thoroughly mixed with a dried powder of IR grade potassium bromide material with weight ratio of 3:1 (i.e 9 mg of KBr in 1 mg of drug). The mixture of materials was pressed using a hydrostatic press at a pressure of 10 tons for 5 min at room temperature with required humidity. The disc of sample was placed in the sample holder for measuring the spectrum and the spectra were recorded as the wave number ranges 4000-400/cm at a resolution of 4/cm. The compatibility i.e. drug-excipients interaction studies are helpful for dosage form design. For compatibility studies drug / excipients ratio are selected and investigated based on the reasonable drug / excipient ratio in the final product. Drug and other Excipients were weighed as 1:1 ratio and passed through sieve # 40, mixed well. The blend was filled in amber color glass vials and stopped with grey rubber stoppers followed by aluminium seal [13].

Preparation of the haloperidol transdermal patch: The objective of present study was to prepare transdermal film containing haloperidol able to release drug within short time interval. The sodium alginate and methyl cellulose solutions were prepared separately by dissolving the required quantities in distilled water, whereas chitosan solution was prepared by dissolving the polymer in 1 % v/v acetic acid solution with stirring at 40 °C. The API haloperidol quantity 20 mg were dissolved in casing solvent before addition of polymeric solution separately as given in Table 1. The drug polymer mixture was continuously stirred on thermostatic magnetic stirrer at 37±2°C. The plasticizers Glycerin/ PVP/ PEG400 were added with stirring. All the solutions were allowed to stand overnight to remove the air bubbles. After stirring completion, it was sonicated in ultrasonic water bath and poured in petri dishes containing mercury base having circular glass bangles with open at both sides. The bottom of the bangle was wrapped with aluminum foil to allow solvent evaporation at 35°C (Olven Instruments, India). The films were prepared by solvent casting method. The dried films were separated, cut into circular films of 2 cm2 (4 mg drug), wrapped in aluminum foil and stored in air tight polyethylene bags in desiccators [14].

Table 1: Preparation of haloperidol containing transdermal patch

Formulation Code	Polymers (gm)		Plasticizers	
	HPMC	Gum tragacanth	Glycerin (ml)	PVP (gm)
HTP1	2	-	5	-
HTP2	-	2	5	-
HTP3	1	1	5	
HTP4	2	-	-	1
HTP5	-	2	-	1
HTP6	1	1		1

Evaluation of transdermal film:

Physical appearance: The parameters i.e. “optical checking, smoothness, color, transparency and flexibility” were observed**.**

Thickness: Measurement of polymeric films thickness was performed by utilizing a screw gauge (least count of 0.02 mm)**.**

Weight variation: Prepared polymeric films were weighed cautiously in triplicate manner and calculated the mean. The weight of individual films should be within permitted limit the mean weight of films.

Surface pH: Digital pH meter was used to determine the pH of surface of prepared films. The prepared film piece was cut and kept in 0.5 ml double distilled water and allowed to swell for 1 h.

Tensile strength: Tensile strength of 2 cm^2 film was measured by using fabricated tensile strength apparatus. The films were fixed by tapes and placed in the film holder. The weight required to break the film was noted as break force and tensile strength calculated by the following formulae.

Tensile strength (N / mm^2) = Breaking force (N) / Cross sectional area of sample (mm^2)

Folding endurance: Folding stamina of prepared film was ascertained by manual method as cutting a portion of film. The cut piece or portion of film was folded at the same place. The folding procedure was performed repeatedly till the film broke. Folding endurance were calculated mean of the number of times the film was folded at the same place without breaking**.**

Moisture content: The films were weigh, dried with current of air at 60ºC and were kept in desiccators having calcium chloride at 40ºC for 24 h. Then dried films were kept at room temperature and temperature 75 ± 0.5% Relative humidity (75% humidity maintained by saturated solution of sodium chloride during storage till equilibrium, weighed films, calculated the increase in weight percent**.**

Swelling Ratio: Films were placed in petri dish having distilled water till film achieved constant weight, which as ascertained by weighed the film at a certain time interval. Degree of swelling (SR %) was calculated using the below equation.

SR (%) = [Mass of films at time of investigation – Initial mass of films * 100

Initial mass of films]

Drug content: Square piece of prepared film (2^2 cm) placed in of dissolution medium (100 ml), stirred constantly for 24 hour. The resulting mixture was ultrasonicated for 15 min, filtered. Filtrate was diluted with same dissolution medium and subjected to UV spectrophotometermethod for drug content determination.

***In vitro* skin permeation study (Bhattacharya and Ghosal, 2000):** In vitro drug release study was performed using distilled water in a glass Franz-diffusion cell. The prepared formulations films 2 cm^2 were cut and were uniformly spread onto the cellophane membrane in between donor and receptor compartments of the diffusion cell and were held tightly by springs. The volume withdrawn was replaced with an equal volume of fresh, prewarmed (37±5ºC) phosphate buffered saline (pH 7.4). The resulting aliquates was ultrasonicated for 15 min, filtered. Filtrate was diluted with same dissolution medium and subjected to UV spectrophotometer method for drug content determination.

3. RESULT AND DISCUSSION

The absorption maxima (λ-max) of haloperidol (10 µg / ml) in pH 7.4 phosphate buffer solution were found to be at 221 nm respectively. The spectrum peak point graph of absorbance of drug vs. wavelength is shown in Figure 1. Haloperidol was estimated in-vitro by reported UV spectrophotometric methods. The reported UV spectrophotometric methods were slightly modified and optimized according to the existing laboratory conditions. The drug was estimated in the dissolution medium (pH 7.4 phosphate buffer). The calibration curves in the various dissolution medium (pH 7.4 phosphate buffer) were prepared with drug solutions of known concentrations. The absorbance was measured and plotted against drug concentration (Figure 2). The calibration curves show excellent linearity of data as evidenced by the values of correlation coefficients that were found to be greater than 0.99. The curves were found to be recti-linear in the concentration range 10 µg / ml to 50 µg / ml for the drug. The percent relative standard deviation was found to be less than 1 % i.e. the method was precise. The recovery of drug from pH 7.4 phosphate buffer was estimated. Quantitative recoveries were recorded for the drugs, ranging from 99.02 to 100.88 %. The estimation procedures for drugs were found to be sensitive, precise and reproducible.

The sensory evaluation test of drug sample i.e. white color, odorless and slightly bitter in taste. The drug sample Haloperidol was white in color, odorless and slightly bitter in taste and were crystalline in nature. The particle size of unmilled Haloperidol was to be 82 µm. The flow properties of drug powders result was concluded that unmilled powders have good to passable type of flow in nature. The solubility of Haloperidol at Water, 0.1 N HCl, Phosphate buffer pH 4.5, Phosphate buffer pH 6.8 and Phosphate buffer pH 7.4 were 1.323 (mg / ml), 1.786 (mg / ml), 0.821 (mg / ml), 3.122 (mg / ml)and 1.061 (mg / ml) respectively. The results were shown in Table 6.10. The partition coefficient of haloperidol was found to be 1.93. The melting point of drug sample haloperidol was 123ºC. The interpretation of IR study spectrum is shown in Figure 3 – 4. The FTIR spectra of pure Haloperidol illustrated sharp distinctive peaks at 1193 (C-N stretch), 1024 (C–C stretch), 1541 (C=C 117 stretch), 1396 (Carboxylate anion stretch), 1735 (C=O stretch), 3279 cm-1 (N–H stretch) and 2879, 2941(C–H stretch).

Characterization of haloperidol patch: The prepared haloperidol patch were characterized a number of optimized parameters i.e. “optical checking, smoothness color, transparency and flexibility, Thickness of polymeric films, Mass deviation of films, Uniformity or texture of films, Surface pH of films, Tensile strength of films, Cracking acceptance

power of films, Water ingestion amount of films, Swelling Ratio of films, Wetness of films". The values obtained after the examination identified by in-vitro drug release study (58.34 – 95.37 %), that polymers chitosan have hydrophilic nature and able to enhanced spreadability and dispersibility of the water-soluble haloperidol. The hydrophilic polymer layer produces a water-permeable with more hydrated film. Such hydration allows losing the polymer matrix and consequently enhanced drug release more than 95.5% within a 6 - 7 h as needed for immediate release. The polymeric films (HTP3) were selected on the basis of its physical appearance, tensile strength, percentage elongation, folding endurance, swelling ratio, moisture content, moisture uptake nature, drug content and in-vitro drug release study parameters. The release kinetic study confirmed the prepared patch was followed supercase II transport mechanism of diffusion kinetics (Table 6.22 – 6.38 and Figure 6.26 – 6.33) with sustained release within specific time period. Regression analysis was performed and the r^2 values suggested that the curves were fairly linear and slope values were computed from the graph. The release exponent "n" values were in the range of 1.033 to 1.169 (Table 6.39 – 6.40). The release exponent "n" was > 1.0 indicating Super-case II transport mechanism and observed deviation from Fickinan mechanism of drug release.

4. CONCLUSION

Many approaches have been developed and are still under process to achieve transdermal delivery. A transdermal patch is a common way of delivering drugs, which consists of an adhesive that leads to the dispersion of the drug, and the membrane in the patch regulates the drug release from the reservoir.

Table 2: Outcomes of repeatability test of 10 µg / ml drug solution for haloperidol

S. No.	Drug content of haloperidol (λ-max 221 nm)
1	0.182
2	0.181
3	0.182
4	0.183
5	0.181
6	0.181
7	0.182
8	0.181
9	0.182
10	0.181
Mean	0.182
Standard Deviation	0.00086
% RSD	0.0118

Table 3: Outcomes of intra-day precision test of 10 µg / ml drug solution for haloperidol

S. No.	Time (h)	Drug content of haloperidol (λ-max 221 nm)
1	0	0.181
2	1	0.182
3	2	0.182
4	3	0.183
5	4	0.181
6	5	0.182
7	6	0.181

8	Mean	0.182
9	Standard Deviation	0.00034156
10	% RSD	0.12471

Table 4: Outcomes of inter-day precision test of 10 µg / ml drug solution for haloperidol

S. No.	Time / Day	Drug content of haloperidol (λ-max 221 nm)
1	Day 1	0.183
2	Day 2	0.182
3	Day 3	0.181
4	Mean	0.182
5	Standard Deviation	0.0124
6	% RSD	0.12431

Table 5: Outcomes of accuracy test for haloperidol

S. No.	Recovery level (%)	Drug recovered (mg)	Drug added (mg)	Drug recovered (%)	Mean	SD	%RSD
1	25	24.56	25	99.88	99.82	0.2119	0.1586
		24.21	25	98.98			
		24.01	25	99.16			
2	50	48.15	50	99.97	100.19	0.3129	0.0464
		48.95	50	99.88			
		49.15	50	100.09			
3	100	99.92	100	99.59	99.59	0.1121	0.0535
		99.96	100	99.56			
		99.93	100	99.62			

Table 6: Characterization of haloperidol single layer transdermal patch

Formulation code	Thickness (mm)	Average weight (mg)	Folding endurance	Percentage Elongation	Tensile Strength N/mm^2	Swelling ratio (%)	Surface pH	Drug content of films (%)

HTP1	HTP2	HTP3	HTP4	HTP5	HTP6
0.29±0.03	0.26±0.02	0.25±0.03	0.24±0.02	0.23±0.01	0.22±0.01
111.32.±1.154	110.33±1.156	112.60±0.144	119.23±1.154	118.33±1.155	114.66±1.165
93-97	94-98	99-101	92-95	78-71	82-72
93.74±0.15	94.81±0.02	101.42±0.09	116.52±0.02	118.12±0.03	119.11±0.02
3.66±1.18	6.69±0.23	5.93±0.13	6.79±0.23	5.86±1.18	6.13±0.13
23.97±0.43	22.32±0.39	22.18±0.58	21.43±0.49	19.42±0.57	16.63±0.54
5.5 ± 0.14	5.6 ± 0.14	5.7 ± 0.12	5.8± 0.12	5.5 ± 0.13	5.5 ± 0.14
93.99±0.8	94.95±0.9	95.79±0.10	99.59±0.11	98.07±0.12	99.85±0.13

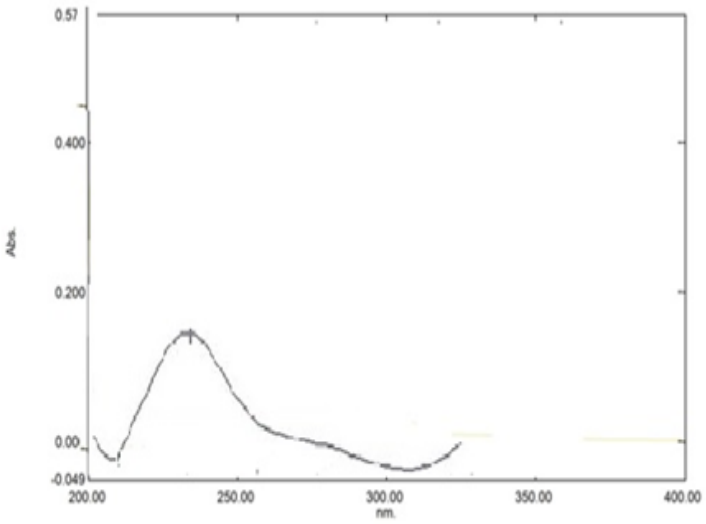

Figure 1: Absorption maxima (λ-max) of haloperidol in phosphate buffer pH 7.4 solution (10 µg/ml)

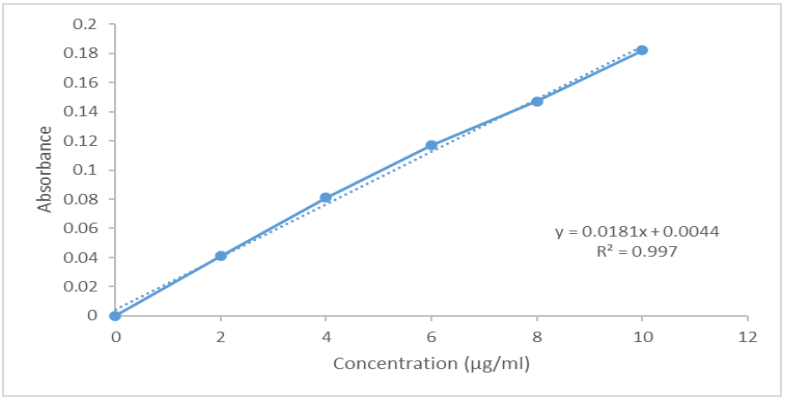

Figure 2: Standard curve of haloperidol in phosphate buffer pH 7.4 solution (221 nm)

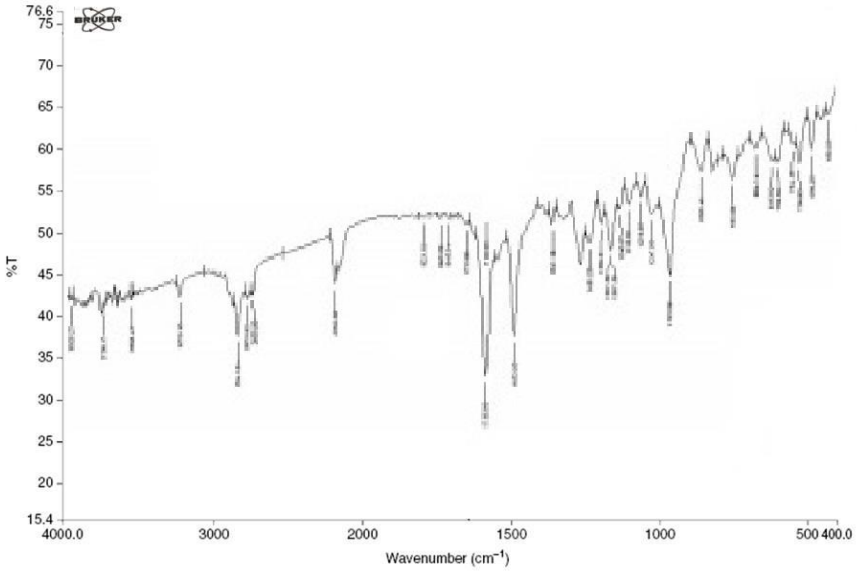

Figure 3: I. R. Spectrum of haloperidol sample (S1)

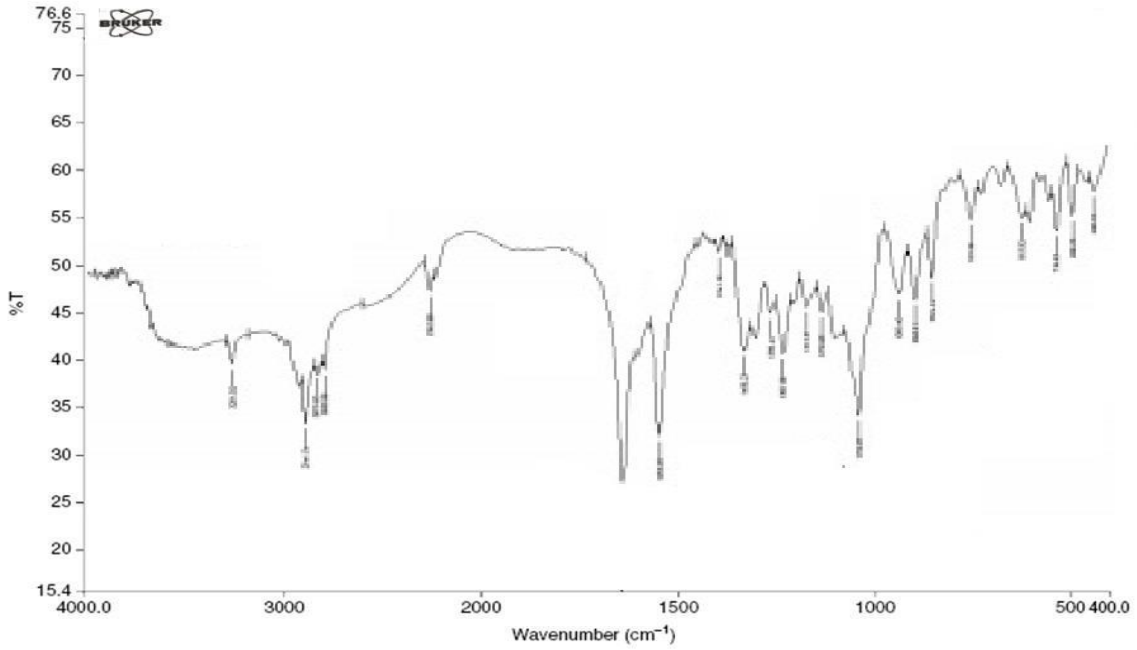

Figure 4: I. R. Spectrum of Haloperidol drug and all excipient (S2)

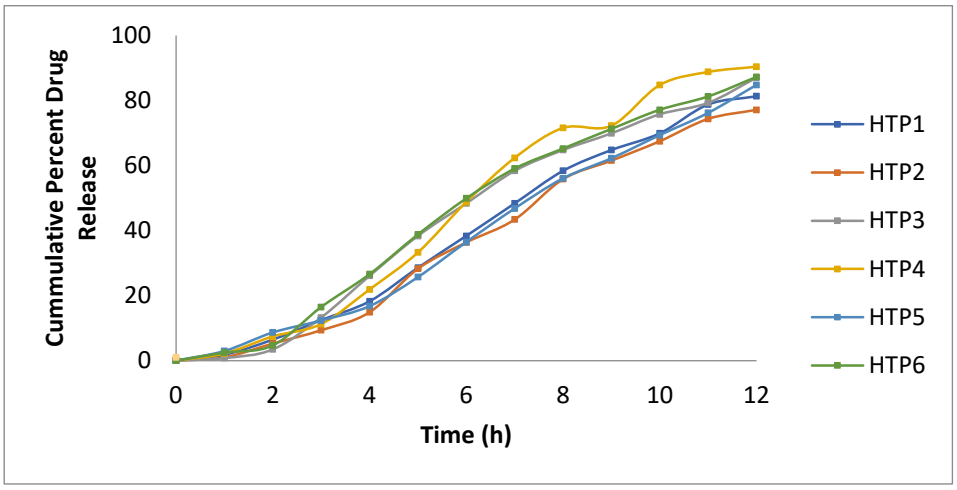

Figure 6: in-vitro release kinetic study of haloperidol single layer transdermal patch

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