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Development And Evaluation Of Matrix Type Transdermal Patches Of Donepezil

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ABSTRACT

The present study focuses on the formulation and evaluation of matrix-type transdermal drug delivery systems (TDDS) of Donepezil, a drug commonly used in the treatment of Alzheimer's disease. TDDS offers numerous advantages over traditional drug delivery systems, including controlled release, improved patient compliance, and avoidance of first-pass metabolism. In this study, ten different transdermal patch formulations of Donepezil were developed using the solvent evaporation method with various combinations of polymers such as HPMC, ethyl cellulose, chitosan, and PVP K30. Preformulation studies, including melting point, solubility analysis, partition coefficient determination, and FTIR spectroscopy, were conducted to assess the drug's physical and chemical properties and compatibility with selected excipients. The patches were characterized for physicochemical properties such as thickness, weight uniformity, folding endurance, moisture content, drug content, and water vapor transmission rate (WVTR). In-vitro drug release studies were conducted using Franz diffusion cells and UV spectroscopy, and release kinetics were evaluated. Among the formulations, patch P4 exhibited the highest drug release (71.28%) over 7 hours and was found to be stable under accelerated stability conditions. Release kinetics followed the Korsmeyer-Peppas model, indicating a diffusion-controlled mechanism. The study concludes that the matrix-type TDDS of Donepezil, especially formulation P4, demonstrates potential for sustained drug release and improved therapeutic efficacy in treating cognitive disorders.

Keywords: *Donepezil, Transdermal Drug Delivery System (TDDS), Matrix Patch, Controlled Release, Polymers, Franz Diffusion, In-vitro Evaluation, Drug Release Kinetics.*

1. INTRODUCTION

In current scenario, there are so many updates in the technology of formulation of dosage forms. New research target for new dosage development by using existing drugs[1]. TDDS offer so many advantages over the conventional dos. form. TDDS also many limitations of the parenteral dosage forms like avoidance of the pain during administration of the dose, and self medication, there will be less fluctuation in the drug plasma concentration[3]. As far as risk factors are concerned it has less risk as compared with others moreover self-administration is possible thus it leads to patient compliance[4]. Controlled drug release is possible, with less fluctuation of the blood concentration[5].

Patches are suitable to use in these conditions [11-17]:

1. Patient with intolerable side effects like constipation.
2. Patients can't use oral medication due to dysphagia.
3. Patient with cognitive impairment.
4. Patient unfit for self-medication.

Care in usin patch18[-23]

1. Use patch on skin after proper cleaning.
2. There should be no any cut on the patch.
3. Before applying new patch, old one should be removed.
4. Care should be there in removal or applying the patch.
5. Accuracy should be there while applying at the required area.

Principle of TDDS:

Skin largest organ and is a barrier for exogenous substances, plays important role in entry to active substance in to body. Skin serve as organ having different responsibilities like sensory, temperature regulation, protective, absorption, excretion[29]. Several molecules crosses this horny layer and the main focus of researchers are on the increase in the penetration of skin by several means[20]. Hydrophilic substances have poor permeability across the membrane because of the presence of lipid matrix[21].

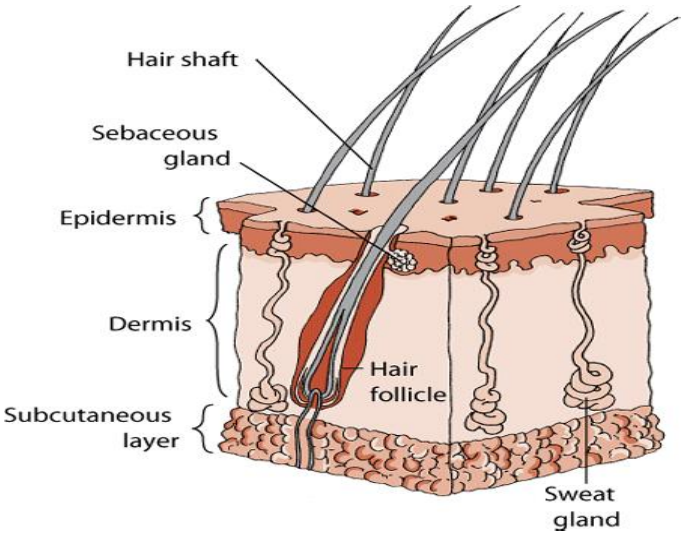


Figure 1: Structure of Skin

Basic components

1. Polymers26:

There are so many polymers that are used in the TDP, for release control. Polymers should possess following properties-

1. Optimum mol wt favouring diffusion
2. Stable should have long shelf life.
3. Non-toxic
4. Inexpensive/ economical.
5. Capable to hold large amount of drug within the system.
5. Compatible with other ingredients.
6. Capable to control the release of drugs.

Natural Polymers: These are obtained from the natural resources, examples includes chitosan, gelatin, natural rubber, waxes, gums, and cellulose derivatives etc11.

Synthetic Polymers: Obtained through various chemical reaction and different procedures, examples includes- PVA, PVP, PEG, Eudragits, EC, HPMC, polyurea.

Drug47:

As far as drug selection for the TDDS are concerned, it should posses following properties to get maximum benefits of this system-

1. High first pass effect.
2. Poor self life.
3. Dose<25mg/day
4. Low mol. Wt (<500 Daltons).
5. Low M.P. (<200°C)
6. 1<log P<3

Permeation enhancers

These are for promotion of permeation across the skin. Examples includes, some solvents like Dimethyl sulfoxide, Ethanol, Propylene glycol, Methanol, etc. Anionic surfactants like SLS are also used for this purpose, some essential oils like Linoleic acid, Caraway oil, Lemon oil are also posses such properties to enhance permeation18.

PSA (Pressure Sensitive Adhesives)

PSA are for maintaining contact with TDS and surface of skin. These stick to skin by applying gentle pressure. After removal it should not leave any residue. Examples includes polyisobutylene, and Polyacrylates21.

Backing Laminate:

There is a inert layer that is used to support mechanically any TDP and that prevents back flow of the drug. It should provide sufficient flexibility, and transmission of oxygen and transmission of water vapour. Polyster film, polyurethane film, and ethyl vinyl copolymer are used as backing membrane18.

Release Liner: TDP with drug is covered with a protective liner that is to be remove just before it's application to the skin. This play important role during storage of the formulations. Examples are polyvinylchloride. Other materials includes metallized laminates and polyester foil22-25.

Types of TDP

1. Membrane permeation controlled TDP:

Drug get permeated through membrane in a controlled manner. Examples of this type are Estraderm, Transderm-Scop etc[23].

2. Matrix Diffusion controlled system:

In these systems, hydrophilic or lipophilic polymers are used to incorporate drug to make reservoir. Prepared drug reservoir is moulded into a disc of fixed surface are and used with occlusive base plate. Example includes Nitro-Dur System[24].

3. Adhesive Dispersion system:

Drug reservoir is arranged by the means of dispersion of drug in adhesive polymer like Polyisobutylene. Examples of such system includes Deponit[24].

4. Microreservoir type systems: In these systems reservoir of drugs is formed by mixing drugs in aqueous solution having polymers. Further it is added with lipophilic polymers with shearing so that micro reservoirs in large quantities can form. This prepared medicated disc is placed in between medicated disc and adhesive pad[11-16].

2. AIM AND OBJECTIVES

TDDS is a way of drugs delivery through skin that is accessible largest organ to move the drug to systemic circulation through its layers. Several advantages are associated with TDDS that make it important way, as some limitations associated with oral and parenteral routes can be eliminated by means of it like pain at the time of administration in parenteral products and first pass metabolism as in oral routes. It provides patients compliance for and reduces side effects associated with drug. It reduces the frequency of drug administration like in oral routes.

Donepezil was used in the present study. It absorb slowly through git after its oral administration. It have T_{max} value in between 3 to 4 hrs,

Objectives includes

1. Preparation of matrix type TDP of Donepezil.
2. Control the release, so that frequent administration can be avoided.
3. To avoid side effects associated with oral administration.
4. Evaluation of pharmacokinetics of Donepezil with the formulations of this study.
5. To check the suitability of new formulation on the basis of results.
    a. General physical characteristics
        i. Thickness
        ii. Weight uniformity
        iii. Content uniformity
        iv. % ML(moisture loss)
        v. % MC (moisture content)
        vi. % MA (moisture absorption)

vii. WVTR
viii. Flatness
ix. FE (Folding endurance)

b. *In-vitro* % release of drugs

3. RESOURCES AND METHODOLOGY

Table 1: Chemicals used in research work

Sr. No.	Chemical	Supplier
1.	Donepezil	Mylan laboratories limited, Hyderabad, Andhra Pradesh (Gift sample)
2.	PG (Propylene glycol)	CDH, Delhi
3.	Glycerine	CDH, Delhi
4.	Chitosan	Central Institute of Fisheries, Cochin. (Gift sample)
5.	PVP K30	CDH, Delhi
6.	Triethanolamine (ml)	CDH, Delhi
7.	*Sodium lauryl sulfate*	CDH, Delhi
8.	Di-Sodium Hydrogen Phosphate aR	CDH, Delhi
9.	Ethanol	CDH, Delhi
10.	HCl	CDH, Delhi
11.	Octanol	CDH, Delhi
12.	Sodium Hydroxide pellets	CDH, Delhi

Table 2: Equipments used in research work

S N	Equipment	Source
1.	Franz Diffusion Cell	Locally Fabricated
2.	Scanning Electron Microscope	JEOL, Japan
3.	Franz diffusion cell	Delhi
4.	Dessicator	Biocraft, M.P
5.	Screw gauge	Ambala Cantt
6.	DSC instrument	NETZSCH, DSC-204 F1 PHOENIX
7.	Electronic Balance	Shweta Scientific, Lucknow
8.	Magnetic stirrer	Shweta Scientific, Lucknow
9.	pH – Meter	Shweta Scientific, Lucknow
10.	Hot – air oven	Shweta Scientific, Lucknow
11.	UV Spectrophotometer	Lasani
12.	Sieve Shaker	Shweta Scientific, Lucknow

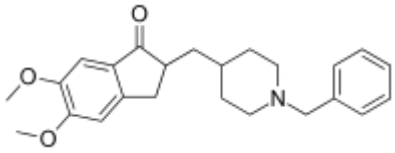
13.	FTIR	Perkin

Donepezil

Nomenclature

• **Name**	Donepezil
• **IUPAC**	(*RS*)-2-[(1-Benzyl-4-piperidyl)methyl]-5,6-dimethoxy-2,3-dihydroinden-1-one
• **Trade Names**	Adlarity

Formula

• **Empirical Formula**	$C_{24}H_{29}NO_3$
• **Structural Formula**	

Physical and chemical properties[6,7,8]

Molecular weight	379.500 g·mol^{-1}
Color	White
Nature	Crystalline
Odour	Odorless
Melting point	223-227°C
Taste	Bitter
Solubility	Insoluble in H_2O, freely in chloroform, methanol, & ethanol.
log P	4.46
PKa	14.91 (strong acidic)

Pharmacokinetics-

After oral administration, Donepezil is absorbed with a slow speed via g.i.t. It has Tmax valued in between 3 to 4 hrs. It can cross BBB and CSF barrier and used for the CNS disorder treatment.

It undergoes presystemic metabolism in liver[89].

Mechanism of action

Donepezil bind and inhibit cholinesterases, particularly acetylcholinesterase, and inhibit its hydrolysis. Due to it, concentrations of acetylcholine increases on cholinergic synapses[90,91].

Medical uses

Donepezil used in the case of dementia, that is a stage of memory loss, with Alzheimer's disease. It improve the ability of thinking in the patients.

Adverse Reactions

- Appetite loss.
- weakness

- Cramping of muscle.
- Nausea
- Diarrhea
- Vomiting
- Sleeping trouble

Preformulation Studies:

Solubility analysis

Ten gm of drug sample was mixed with 10 ml solvents. Shaking for 2hr was provided to test tubes to dissolve the drug completely. After it solution was filtered and was analyzed through UV spectcrophotometer (322 nm)[17].

M.P. determination

Thiels tube method was used for estimation of Melting point. 300 ml paraffin was placed in Thiels tube, and sealed by means of flame. Thermometer was used to noted temperature [8-10].

Partition coefficient

Aqueous phase was prepared by buffer (pH 7.4) and water and n-octanol was used as oil phase. Both phases taken equally and 100 mg of Simvastatin was added and mixed by the means of a shaker for 6 hrs. Phases were separated by separating funnel and analyzed through UV Spectrophotometer (322 nm).

The PC was calculated using this formula [25-28].

$$\text{Po/w} = \frac{\text{Concentration in octanol}}{\text{Concentration in phosphate buffer pH 7.4}}$$

FTIR analysis

FTIR spectroscopy was used to check any compatability issue of the Simvastatin with polymers. This is an important testing as it is related with the stability of the formulations. Simvastatin and polymers were kept in vials of ambered color for the removal of the moisture. FTIR testing of samples was carried out by the means of pellet making method by using KBr[10].

Calibration curve preparation in methanol

Calibration curve was plotted by taking phosphate buffer (pH=7.4) as the solvent. Subsequently, many dilutions were made using the previous solution. Different amount of buffer was taken and diluted to prepare different concentration to check the absorbance by the means of UVspectrophotometer at the maximum wavelength 232 nm.

Formulation development:

Total 10 formulations prepared by the means of use of polymers in different ratio as in Table 2 through solvent evaporation technique12.

Evaluation **of TDP**

Physical Properties

1. Thickness[13]

2. It was measured by means of Screw gauge.

2. Weight

Average weights of the different patches were estimated[26].

3. Content Uniformity

3. It was measured by means of finding absorbance by UV Spectrophotometer by dissolving the patches in buffer[13].

4. Folding Endurance

Patch was taken and folded many times at same place until it gets breakage[14].

5. % ML (% Moisture Loss)

It was measured with the use of Dessicators (80-90%RH). It was measured in 3 different days[16].

$$\% \text{ ML} = \frac{\text{WI} - \text{WF}}{\text{WI}} \text{X100}$$

WI= Initial Wt, WF= Final Wt

6. % Moisture Content

Dessicators with 80-90%RH was used for this study[15].

$$\% \text{ Moisture content} = \frac{\text{WI} - \text{WF}}{\text{WI}} \text{X100}$$

WI= Initial wt, WF= Final wt

7. % MA (Moisture Absorption)

Dessicators with 80-90%RH was used for this study[15].

$$\% \text{ Moisture absorption} = \frac{\text{WF} - \text{WI}}{\text{WI}} \text{X100}$$

WI= Initial wt, WF= Final wt

8. WVTR (Water vap. transmission rate)

1 gm $CaCl_2$ was placed in a vial, having patch of area 2.076 cm^2 at brim. It was placed in a desiccators to measre the change in wt for 7 days[17].

$$\text{WVTR} = \frac{\text{WF} - \text{WI}}{\text{TXA}} \text{X100}$$

Where, WI=Weight Initial, WF= Weight Final, T=Time, A= Area

9. Flatness

Flatness uniformity was estimated as-

$$\text{Constriction (\%)} = \frac{\text{LF} - \text{LI}}{\text{LI}} \text{X100}$$

Where, LF = length final, and LI = length initial

***10. In-vitro* drelease:** Franz diffusion cell was used for it. Patch was placed in between donor and receptor compartment. Buffer was place in receptor compartment, sample was withdrawn and check by UV spectrophotometer for the change in drug conc. At 250 nm[10].

11. Release kinetic:

It was done through PCP disso software[11].

12: Stability study

Formulations of batches MTP1, and MTP5 were subjected to different conditions for estimation of its effect on the concentration. Conc. Was measured by means of UV spectrophotometer[6].

4. RESULTS

Table 3: Donepezil calibration curve (buffer pH 7.4).

Conc. (µg/ml)	Abs.(Mean±S.D), N=3
0	0
1	00.098±00.06
2	00.164±00.04

3	00.230±**0**0.07
4	00.352±**0**0.21
5	00.461±**0**0.09
6	00.552±**0**0.24
7	00.634±**0**0.14
10	00.752±**0**0.08

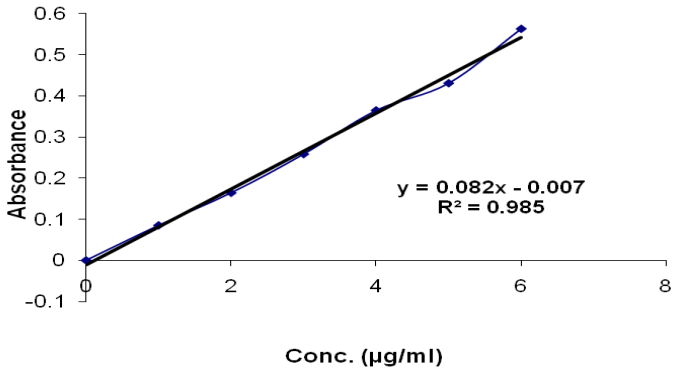


Figure 3: Donepezil calibration curve (buffer pH 7.4).

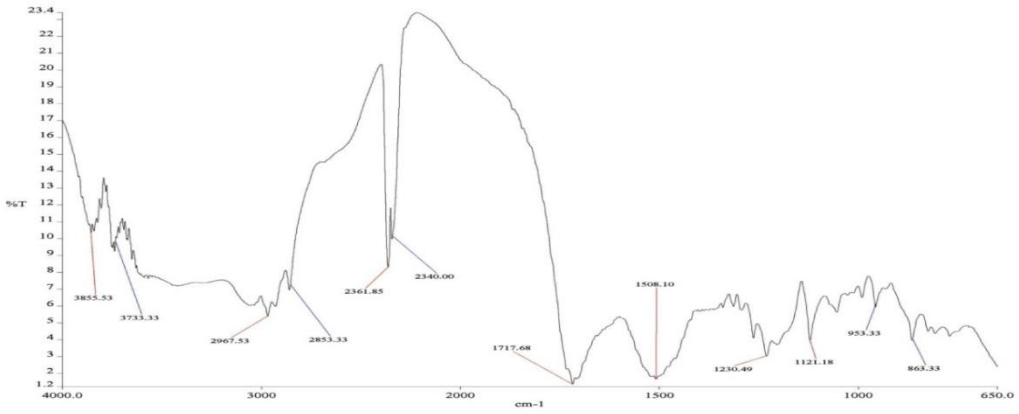


Figure 4: Donepezil FTIR.

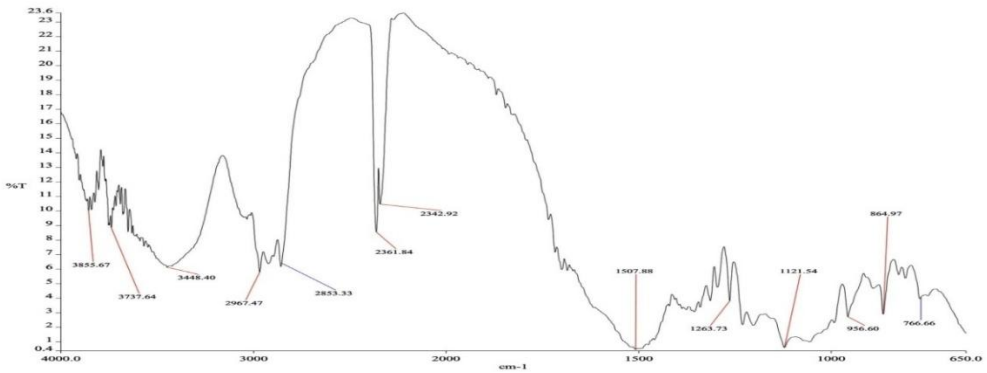


Figure 5: Donepezil and Chitosan, PVP K30, Ethyl cellulose and HPMC mixture FTIR spectrum.

Table 4: Melting point of drug

Received sample	Melting point
	223-227°C

Table 5: Compositions of patches

Batch	Donepezil (mg)	Polymers	Solvent (w/v)	Plasticizer
P1	300	PVP K30:Chitosan::30:70	AA(1%)	PG (30%)
P2	300	PVP K30:Chitosan::50:50	AA (1%)	PG (30%)
P3	300	PVP K30:Chitosan::70:30	AA (1%)	PG (30%)
P4	300	PVP K30:Chitosan::85:15	AA (1%)	DBP (30%)
P5	300	Ethyl cellulose:Chitosan :: 30:70	AA (1%)	DBP (30%)
P6	300	Ethyl cellulose:Chitosan:: 50:50	AA (1%)	DBP (30%)
P7	300	Ethyl cellulose:Chitosan:: 70:30	AA (1 %)	Glycerine (20%)
P8	300	Ethyl cellulose:Chitosan:: 85:15	DM (2%)	PG (30%)
P9	300	PVP K30:HPMC::30:70	DM (2%)	Castor oil (20%)
P10	300	PVP K30:HPMC::50:50	DM (2%)	PG (30%)

AA= Acetic acid; PG= Propylene glycol; DBP= Dibutylphthalate; DM= Dichloromethane

Table 6: Characterization of patches.

Batch Code	Physical Appearance	Thickness (mm) ± SD	Mass Uniformity (mg)	% Drug Content	% Moisture Content
P1	wrinkled	.039±.41	48.6±0.09	94.42± 0.12	2.75±.09
P2	Smooth	.036±.09	45.5±.12	98.42± .09	2.79±.16
P3	Smooth flexible	.042±.21	44.3±.08	95.42± .09	2.89±.16
P4	Hard and tough	.039±.08	46.7±.08	94.52± .21	2.75±.13
P5	tough	.038±.19	47.9±.11	97.35± .32	2.65±.15
P6	tough	.043±.09	46.7±.14	96.62± .12	3.53±.64
P7	Smooth	.039±.18	45.4±.15	95.79± .12	3.34±.65
P8	flexible	.042 ±.31	46.1±.18	94.65± .12	3.68±.21
P9	Smooth	.053±.09	43.2±.23	95.31± .15	3.45±.24

P10	flexible	.038±.19	46.7±.11	96.31± .32	2.55±.16

Table 7: Characterization of patches-2

Batch Code	% Moisture Absorption	% Moisture loss	WVTR ($g/cm^2/hrs$	Folding Endurance	Flatness %
P1	6.542±.07	2.781± .09	$2.427X10^{-4}$± .11	> 264	100
P2	5.428±.89	3.552±.08	$2.528 X10^{-4}$± .13	> 245	100
P3	4.455±.09	2.724±.11	$2.731X10^{-4}$±.14	> 274	100
P4	5.582±.11	3.432±.12	$2.847X10^{-4}$± .09	> 288	100
P5	6.884±.09	3.531±.14	$2.732X10^{-4}$± .08	> 275	100
P6	7.208±.21	3.659±.09	$1.558X10^{-4}$±.14	> 257	100
P7	6.331±.32	3.745±.08	$1.771X10^{-4}$±.21	> 272	100
P8	8.232±.41	3.739±.14	$1.662X10^{-4}$±.09	> 267	100
P9	8.408±.09	3.659±.21	$1.458X10^{-4}$±.21	> 270	100
P10	7.684±.11	3.731±.12	$1.732X10^{-4}$± .11	> 267	100

mean±SD, N=3

Table 8: % drug released of batch P1 to P5

Time (Hrs)	% released				
	P1	**P2**	**P3**	**P4**	**P5**
0	0	0	0	0	0
1	6.44±.21	11.26±.45	5.72±.23	24.22±.45	19.26±.09
2	8.93±0.38	24.62±0.53	7.85±0.29	35.48±0.26	26.41±0.08
3	13.26±0.15	32.89±0.32	10.94±0.18	44.58±0.15	41.36±0.011
4	16.65±0.47	36.88±0.28	12.97±0.17	54.32±0.61	48.59±0.07
5	19.09±0.25	41.56±0.50	13.88±0.18	61.55±0.14	54.63±0.05
6	22.71±0.55	50.27±0.48	19.67±0.33	64.39±0.45	60.51±0.13
7	27.64±0.26	54.51±0.35	25.47±0.33	71.28±0.19	68.32±0.17

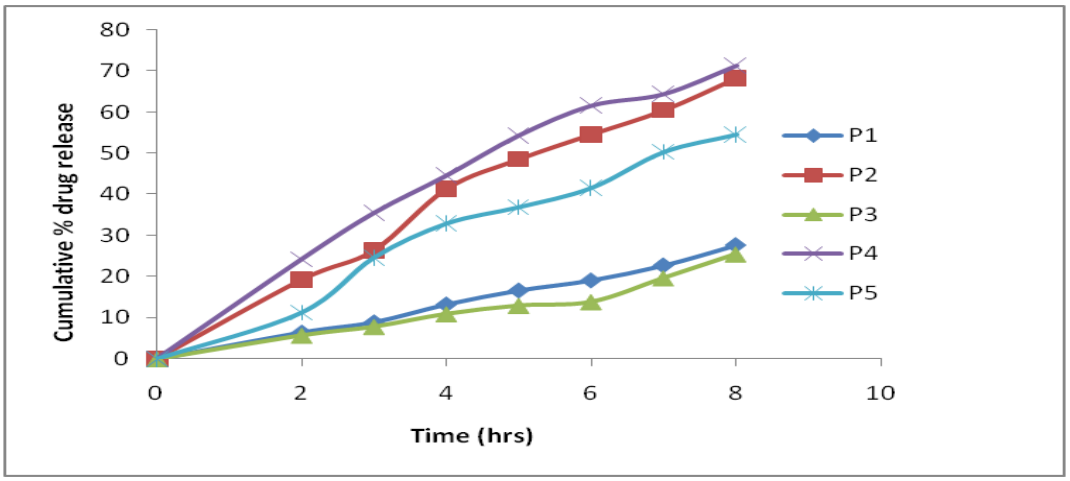


Figure 6: % released of batch P1 to P5.

Table 9: % drug released of batch P6 to P10.

Time (Hrs)	% released				
	P6	P7	P8	P9	P10
0	0	0	0	0	0
1	12.26±.09	17.26±.54	11.44±.32	5.72±.24	21.22±.03
2	22.62±0.08	21.41±0.45	14.63±0.41	7.85±0.13	37.48±0.25
3	28.89±0.09	25.36±036	17.32±0.36	9.94±0.13	46.58±0.41
4	33.88±0.08	41.59±0.47	23.25±0.33	14.97±0.09	56.32±0.35
5	40.56±0.11	49.63±0.51	26.39±0.09	18.88±0.07	59.55±0.36
6	48.27±0.12	57.51±0.41	34.78±0.08	19.67±0.08	63.39±0.26
7	53.51±0.14	62.32±0.19	41.55±0.24	23.53±0.04	66.28±0.38

mean±SD, N=3

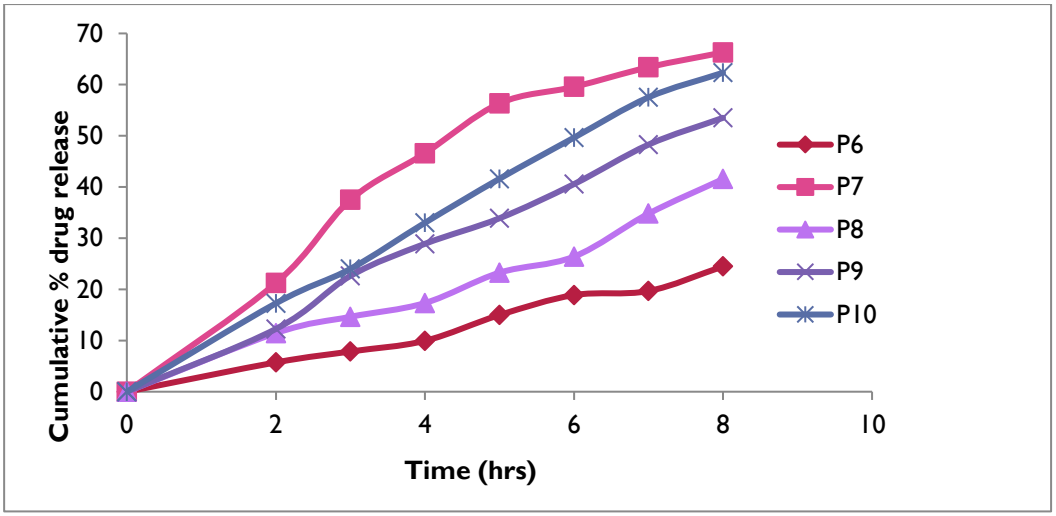


Figure 7: % released of batch P6 to P10.

Table 10: Kinetics models of drug release.

Code	Model	Parameters
P1	Peppas and Korsmeyer	R = 0.984, K1 = 5.2154, n = 0.864
P2	Peppas and Korsmeyer	R = 0.943, K1 = 6.712, n = 0.782
P3	Peppas and Korsmeyer	R = 0.975, K1 = 4.284, n = 0.760
P4	Peppas and Korsmeyer	R = 0.983, K1 = 8.243, n = 0.718
P5	Peppas and Korsmeyer	R = 0.965, K1 = -0.034
P6	First order	R = 0.964, K1 = 3.177, n = 0.864
P7	Peppas and Korsmeyer	R = 0.962 , K1 = 7.642, n = 0.732
P8	Peppas and Korsmeyer	R = 0.961, K1 = 7.442, n = 0.762
P9	First order	R = 0.972, K1 = 5.61, n = 0.760
P10	Peppas and Korsmeyer	R = 0.974, K1= -0.070

Table 11: Stability studies of batch P2 and P4.

Weeks	P2			P4		
	Refrigeration	Room	Oven	Refrigeration	Room	Oven
1	99.83±.03	99.89±.02	98.82±.03	99.86±.03	99.87±.03	98.74±.02
3	99.72±.07	99.84±.06	97.93±.06	99.84±.05	99.77±.04	97.53±.05
6	99.88±.08	99.78±.07	97.73±.05	99.77±.06	99.78±.07	97.48±.06
9	99.65±.09	99.72±.09	97.34±.02	99.69±.02	99.74±.01	97.34±.08
12	99.51±.04	99.69±.07	97.21±.08	99.64±.04	99.65±.08	96.72±.09

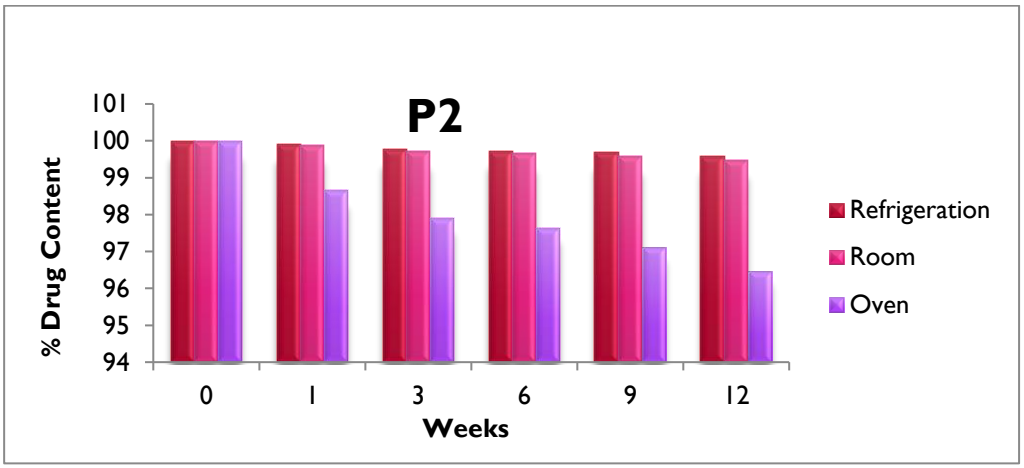


Figure 8: Stability study of batch P2.

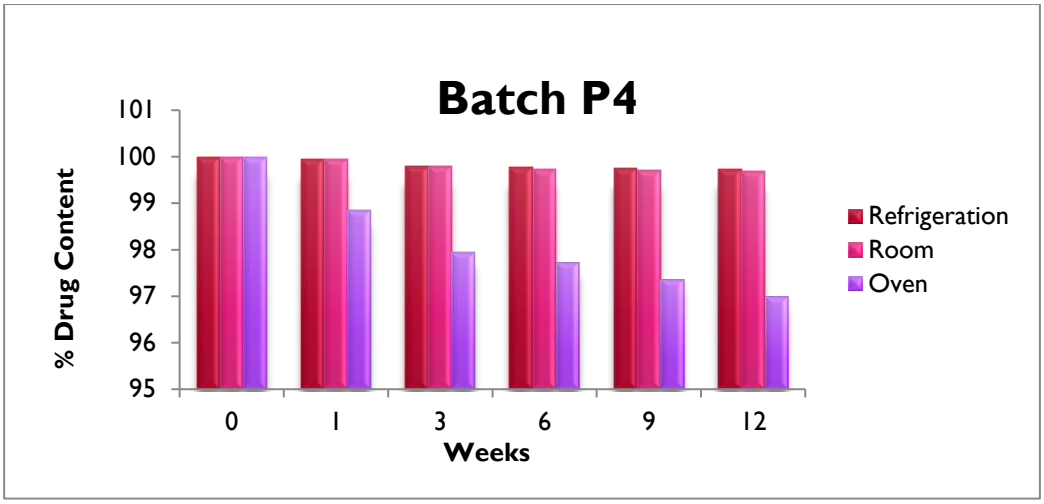


Figure 9: Stability study of batch P4.

5. DISCUSSIONS

Pre-formulation studies: -

Donepezil was obtained from Mylan laboratories limited, Hyderabad, Andhra Pradesh as a Gift sample. For the authentication of the sample, the sample was subjected for thePre-formulation study including i.e., melting point, solubility, FTIR.

Solubility: - Donepezil is easily soluble in water and sparingly in alcohol.

M. P: - The m.p of drug sample was found in the range of 223-227°C.

Calibration curve preparation

Calibration curve was plotted by taking methanol as the solvent. It was compared in official books like IP, confirm the authenticity of the obtained gift sample of the Donepezil .

Compatibility study

Using the FTIR method, a drug and excipient compatibility analysis was conducted. Due to the presence of excipients, the peak values of Donepezil when alone and when combined were almost same although slightly altered. The drug-lipid mixture did not exhibit any peaks that appeared or vanished. Thus it indicate compatibility of the Donepezil with other used ingredients.

Total of 10 matrix patches of Donepezil have been developed by the means of solvent evaporation technique by using HPMC, EC, chitosan, PVP K30.

Prepared patches formulations were examined visually and characteristics were compared to those of the Std. medicine.

Characterization of formulations

Weight was found in between 43.2±.23 to 47.9±.11 mg.

The % drug content was 94.52± .21 to 98.42± .09**.**

Thickness was in between .036±.09 to .053±.09 mm. This may be because of variation in the viscosity of the polymer used.

WVTR was in the range of $1.458X10^{-4}$±.21 to $2.847X10^{-4}$± .09.

% MA was found in between 4.455±.09 to 8.408±.09.

% MC was in between 2.55±.16 to 3.68±.21

% ML was measured in between 2.724±.11 to 3.745±.08

Maximum folding endurance was found >288 which indicate sufficient elasticity of the formulations.

% release

A UV spectrophotometer operating was applied to evaluate the drug's release during various time intervals. The drug release maximum (71.28±.19%) and minimum (24.47±.04%) are indicated by formulations P4 and P6.

Release kinetics: -

Releases of drug kinetic model were used for illustrating the release of drug mechanism. For this, several models are used.

Regression coefficient (r^2) in every formulation was used to identify the best fit model for manufactured Donepezil patches based on the data observed by the kinetic model.

Stability analysis

The chosen patches formulations from batch P4 and P2 were capable of remaining stable at 45°C in addition to refrigerated temperature, according to 12-week accelerated stability experiments. Consequently, the formulations' qualities won't be impacted by keeping them at room temperature.

6. CONCLUSION

Study concludes following: -

(i) Various preformulation tests conducted on a gift sample of Donepezil demonstrate the sample's genuineness.

(ii) Mixture of Donepezil, and polymers, were evaluated for compatibility by means of FTIR. There was no significant change is peak, this indicates compatability.

(iii) By selecting a solvent evaporation process, ten patches formulations of Donepezil were effectively created using multiple ingredients

(iv) Prepared formulations of patches, were assessed on different parameters. The prepared patchess have a good efficiency and produce good yield.

(v) After 7 hrs, drug release is in between 24.47±.04%% to 71.28±.19%. Maximum drug release was shown by formulations P4.

(vi) The data compiled from several models showed that Donepezil patches formulations adhered to Korsemeyer Peppas kinetic models.

(vii) Batch P2 and P4 selected patches formulations are stable up to 45 degrees Celsius, according to 12-week accelerated stability experiments. Without experiencing significant changes, the optimised formulation's stability assessment revealed acceptable properties.

The current study concludes that batch P4 formulation was the best formulation based on several evaluation metrics.

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