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FORMULATION AND EVALUATION OF ORAL FAST DISSOLVING FILM OF MELATONIN

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ABSTRACT

The goal of this study was to improve Melatonin's oral bioavailability and give a faster onset of action by creating an oral fast dissolving film. Melatonin has a low aqueous solubility, and due to first-pass metabolism, its oral bioavailability is only about 33%. Melatonin oral rapid dissolving film was made by solvent casting with HPMC-E5 (film forming polymer), PEG-400 (plasticizer), -cyclodextrin (solubilizing agent), citric acid (saliva stimulating agent), and mannitol (sweetening agent). For the formulation optimization of oral fast dissolving film of Melatonin, a two factor three level factorial design (32) was used, with experimental trials performed on all possible formulations, in which the amount of HPMC-E5 (X1) and amount of PEG-400 (X2) were selected as independent variables (factor) and varied at three different levels: low (-1), medium (0), and high (+1) levels. The dependent variables were percent medication release and disintegration time (response). The thickness, weight variation, folding endurance, weight variation, surface pH, drug content, disintegration time, and in-vitro drug release of each formulation were all assessed. According to the findings, oral fast dissolving film (F6) avoids first pass metabolism, improves oral bioavailability, and has a quick onset of action.

Keywords: Melatonin, oral fast dissolving film, solvent casting method, HPMC-E5

INTRODUCTION

Because it is more convenient, cost-effective, and results to a high level of patient compliance, the oral route is the most recommended route for medication delivery. For paediatric and geriatric patients who are afraid of choking, the oral route can be difficult due to swallowing difficulties. Newer and safer drug delivery systems have been introduced as a result of patient convenience and compliance-oriented research. Because of improved customer choice, rapid disintegration or dissolution, and self-administration possible even without water or chewing, oral fast-dissolving drug delivery methods (fast dissolving tablet, fast dissolving film) have recently gained popularity and acceptability **[1]**.

Fast dissolving drug delivery systems were first created in the 1970s as an alternative to tablets, capsules, and syrups for juvenile and geriatric patients who struggle to swallow traditional oral solid dosage forms. The oral fast-dissolving film is one of these novel ways to promote consumer acceptance by allowing for quick dissolution, self-administration, easy handling, compact packaging, and a pleasing flavour. When an oral fast-dissolving film is applied solely on the patient's tongue and is instantly wet by saliva, the film quickly hydrates and sticks to the application site. Because the penetrability of the buccal mucosa is 4-4,000 times greater than that of the skin, mouth dissolving films have the ability to dissolve the medication in seconds by saliva and bypass first-pass hepatic metabolism. Dissolved pharmaceuticals are then dropped into systemic circulation by the buccal mucosa. Polymers employed in film preparation should be hydrophilic in nature to achieve this. A low loading dose with improved bioavailability should be used **[2]**.

Melatonin (N-acetyl-5-methoxytryptamine) is a circulating hormone produced by the pineal gland during dark phase of the day night cycle. It involves in the sleep wake cycle and synthetic Melatonin preparations have been extensively used in the treatment of primary sleep problems. up to 90% of blood Melatonin cleared by liver in the single passage due to its low and oral bioavailability it’s about less than 33% and making its half-life very short (30-60 minutes). Melatonin has also been proposed as the standard agent for circadian rhythm sleep disorders, such as delayed sleep phase syndrome and non 24-hours sleep wake syndrome etc. To avoid the first pass metabolism responsible for the 90% loss of the oral Melatonin dose and to ensure rapid onset of activity, oral fast dissolving

film has been formulated additionally increase of contact surface and possibility of mucosal absorption **[3]**.

MATERIALS & METHODS

Material:

Melatonin was purchased from Yarrow Chem. Products Pvt. Ltd. β-cyclodextrin was purchased from Yarrow chem. Products Pvt. Ltd. HPMC-E5, PEG-400, citric acid, mannitol was obtained from loba chemicals.

Identification of Drug:

Determination of wavelength (λmax) using U.V. spectroscopy

10 mg of Melatonin was weighed and dissolved into 10 ml ethanol to prepare stock solution (1000µg/ml) from which a 10µg/ml dilution was prepared. Baseline correction was performed using ethanol and sample was scanned between 200-400nm and wavelength of maximum absorbance (λmax) was determined **[4]**.

Melting Point Determination:

A melting point determination equipment was used to determine the melting point of a pharmacological sample. A powdered drug sample was obtained and placed in a thin-walled capillary tube with a diameter of 1mm that was 10-12 cm long and closed at one end. In a melting point apparatus, the capillary was placed and the melting point of the sample powder was measured after the drug sample was heated and melted **[5]**.

Curve of calibration of Melatonin in ethanolic distilled water at 276.2 nm

Melatonin calibration curves were created using a UV visible spectrophotometer (Shimadzu 1800, Japan) in distilled water. To generate a 1000g/ml stock solution of Melatonin, accurately weighed 50 mg of Melatonin was put into a 50 ml volumetric flask and the volume was filled up by mixing co-solvent (ethanol) with distilled water (2:8).1 mL of the stock solution was transferred to a 10 mL volumetric flask, and the remainder of the volume was produced up with solvent to make a 100g/ml solution, then divide it into 5, 10, 15, 20, and 25 g/ml portions. dilutions were prepared. Then each solution was separately analyzed at λmax 276.2 nm **[6]**.

Calibration curve of Melatonin in phosphate buffer pH 6.8 at 276.2 nm

Melatonin calibration curves were created using a Shimadzu 1800 UV visible spectrophotometer in phosphate buffer pH 6.8. To make a 1000g/ml stock solution of Melatonin, 50 mg of Melatonin was accurately weighed and put into a 50 ml volumetric flask, which was then filled with phosphate buffer pH 6.8. From the inventory solution. 1 mL was taken and transferred to a

10 mL volumetric flask, with the remaining volume being filled with solvent.To make a 100 g/ml solution from which 5, 10, 15, 20, and 25 g/ml are extracted.

Solubility studies.

Melatonin solubility in various media (n=3): Melatonin solubility in various media was determined. The equilibrium solubility method was used to determine the value. 5 mL of each solvent was placed in a separate vial in this approach. In vials containing distilled water and phosphate buffer pH 6.8, an excess of Melatonin was introduced. The vials were filled with 12 hours on a mechanical stirrer at 37°C. For the next 24 hours, the solutions were allowed to equilibrate. The answer was Transferred to eppendroff tubes and centrifuged at 2000 rpm for 5 minutes. Each vial's supernatants were filtered. Make adequate dilutions with a 0.45micron membrane filter and examine with a UV visible spectrophotometer (UV1800 Shimadzu, Japan) **[7]**.

Drug-excipient interaction study:

FTIR absorption spectra of Melatonin and excipients were recorded in the range of 400 to 4000cm-^{1} by KBR disc method using FTIR spectrophotometer. FTIR study was carried out for Melatonin and physical mixture of drug with excipients. FTIR spectra of physical mixture of Melatonin with all polymers were compared with FTIR spectra of Melatonin **[8]**.

FORMULATION DEVELOPMENT: -

Preparation of solid dispersion of Melatonin: Solid dispersion of Melatonin was prepared with β- Cyclodextrin in different ratio (1:1, 1:2, 1:3 and 1:4) by physical mixture method. In this method accurately weighted quantity of Melatonin and β –cyclodextrin was taken in morter and pestel. Melatonin and β-cyclodextrin mixed thoroughly in motor by trituration. This mixture was then passed through sieve number #60 **[9, 10]**.

Preparation of oral fast dissolving films:

The oral fast dissolving film of solid dispersion of Melatonin was prepared were HPMC as a film forming polymer, PEG as a plasticizer, citric acid as a saliva stimulating agent, and mannitol as a sweetening ingredient used in the solvent casting procedure. The preparations were prepared as per composition given in **Table 3**. The hydrophilic polymer HPMC accurately weighed and dissolved in distilled water in a beaker and continuously stirred on magnetic stirrer for 2 hours. Then the weighed quantity of Melatonin and β–cyclodextrin solid dispersion, PEG-400, citric acid mannitol in a separate beaker, was dissolved in distilled water before being added to the polymeric solution. and stirred well using a magnetic

stirrer to obtain homogenous solution. This solution was allowed to stand 12 h for the de-areation of the solution. The solution was then cast in petridish and kept in room temperature for 10 to 12 hours. After drying films were removed and cut into area 2×2 cm^2. The film was covered with aluminum foil and stored in desiccator for further use **[11]**.

Optimization of oral fast dissolving film

A 3^2 full factorial design was used for optimization of polymer-plasticizer ratio. In this design, 2 factors were evaluated each at 3 levels and experimental trials were performed in all 9 possible combinations**.** The amount of polymer HPMC (X1) and plasticizer PEG-400 (X2) were chosen as independent variables, with each factor being investigated separately low (-1), medium (0), high (+1) level. Table 1and 2 shows the levels of independent variables and the drug release and disintegration time used as dependent variables (response) **[12]**.

EVALUATION OF ORAL FAST DISSOLVING FILM:

Thickness of films:

The thickness of the film was measured three times with a micrometer screw gauge, and the averages of the three measurements were determined **[12]**.

Weight variation:

For the evaluation of weight variation of the fast-dissolving film of size 2×2cm2 were cut and 3 films of each formulation were taken and weight individually using electronic balance. The average weight was calculated **[13]**.

Folding endurance:

It is a term that refers to a film's flexibility. The number of folds required to break the film or develop noticeable cracks is expressed as the number of folds (number of times the film is folded at the same plain) it gives an indication of brittleness of the film. A small film 2×2cm^2 was subjected to this test by folding the film at the same plane repeatedly several times until a visible crack was observed. The maximum number of times a film could be folded in the same spot before it broke, cracking gave the value of folding endurance **[14]**.

Surface pH:

The surface pH of fast dissolving film was determined to investigate the possible side effects due to change in pH in-vivo, since an acidic or alkaline pH may irritate the oral mucosa. The surface pH was determined by using pH meter. This test was evaluated by placing the film in a petri dish. Then it was moistened with 0.5 ml of phosphate buffer and kept for 30s. The pH was noted after bringing the electrode of the pH meter in

touch with the surface of the formulation and allowing equilibration for 1 min. The average of three determinations for each formulation was taken **[15]**.

Drug Content Uniformity:

The films were evaluated for content consistency. Films with a surface area of 22 cm^2 were cut, placed in 100 ml volumetric flask and dissolve in phosphate buffer pH 6.8. Volumetric flask was shaken continuously for 10 min. Then solution was filtered through whatman filter paper. After filtration, 1 ml of solution was withdrawn from the above solution in 10 ml volumetric flask and dilute up to 10 ml of phosphate buffer pH 6.8. Solution was analyzed by UV spectrophotometer at λmax 276.2 to calculate the concentration of drug present in the film **[16]**.

In-vitro disintegration test:

Disintegration time of fast dissolving film measured by placing the film area (2×2cm2) in a petridish containing 6 ml phosphate buffer pH 6.8. Time required for complete disintegration of the film was noted **[17]**.

In-vitro drug release:

In-vitro drug release of fast dissolving film of Melatonin was studied in USP Type II (Paddle type) dissolution test apparatus using phosphate buffer pH 6.8 (250 ml) as the dissolution medium. Film of area 2×2 cm^2 was cut and fixed to a piece of metal wire slab and placed at the bottom of the dissolution vessel. The temperature was maintained at 37±0.5ºC with paddle speed rotation 50 rpm. 5ml Sample was withdrawn at specific time intervals and the same quantity was replaced with phosphate buffer pH 6.8 to maintain volume of dissolution medium. The sample were filtered immediately through whatman filter paper and analyzed by UV spectrophotometrically at λmax 276.2 for the drug concentration and calculated the % of drug dissolved or release **[17, 18]**.

RESULT AND DISCUSSION

Identification study of drug

Determination of wavelength (λmax) using U.V. spectroscopy

The absorbance maxima of Melatonin in ethanol were found to be 276.2 nm which matches the reported in literature. UV spectrum of Melatonin is shown in **Figure 1**.

Preparation of calibration curves:

The calibration curves of Melatonin in ethanolic distilled water and phosphate buffer pH 6.8 were prepared and shown in **Table 4 & 5** and **Figure 2 & 3** respectively.

Melting point determination:

The melting point of Melatonin was found to be 1170C ±0.001 which was found same as reported in literature.

Determination of solubility of Melatonin

The solubility of Melatonin in distilled water and phosphate buffer pH 6.8 were studied and the results of study are shown below in Table 6. Results of the study suggested the poor aqueous solubility of Melatonin in distilled water & phosphate buffer pH 6.8. The solubility of solid dispersion of Melatonin with β- cyclodextrin (1:1, 1:2, 1:3, 1:4) in distilled water and phosphate buffer pH 6.8 are studied and the results of study were shown below in **Table 7**.

Drug-excipient interaction study using FTIR

FTIR spectrum of Melatonin, physical mixture of Melatonin with HPMC-E5, solid dispersion of Melatonin with β-cyclodextrin, physical mixture of HPMC-E5 with Melatonin and β-cyclodextrin solid dispersion are shown in figure 4, 5, 6, 7 and peaks mention in **Table 8, 9, 10, 11** respectively. FTIR spectrum of Melatonin, physical mixture of Melatonin with HPMC-E5, solid dispersion of Melatonin with β-cyclodextrin, physical mixture of HPMC-E5 with Melatonin and β-cyclodextrin solid dispersion was recorded and it was found in accordance with the reported peaks shown in **Figures 4, 5, 6, 7**. FTIR spectrum of physical mixture of Melatonin with HPMC-E5 showed the major peaks both the components. There were no incompatibility or interaction found between Melatonin and HPMC-E5 in their physical mixture. FTIR spectrum of solid dispersion of Melatonin with the β-cyclodextrin showed the major peaks of both components. There were no incompatibility or interaction found between Melatonin and β-cyclodextrin in there solid dispersion form. FTIR spectrum of physical mixture of HPMC-E5 with Melatonin and β-cyclodextrin solid dispersion showed the major peaks of both the component. There were no incompatibility or interaction found between Melatonin and β-cyclodextrin solid dispersion with HPMC-E5 in their physical mixture.

Evaluation parameters of oral fast dissolving film:

The Fast dissolving films of Melatonin with β-cyclodextrin solid dispersion were evaluated based on thickness, weight variation, folding endurance, drug content, surface pH and disintegration time. The results of the studies are shown below in **Table 12**. In-vitro % drug release data of F1 to F9 formulation of oral fast dissolving film shown below in **Table 13** and In-vitro % drug release graph shown below in **Figure 8**.

Evaluation of optimized formulation:

The Fast dissolving films of Melatonin with β-cyclodextrin solid dispersion were

evaluated based on thickness, weight variation, folding endurance, drug content, surface pH and disintegration time. The results of the studies are shown below in **Table 14**.

In-vitro % drug release study of optimized batch

In-vitro % drug release data of optimized batch formulation of oral fast dissolving film shown below in **Table 15** and In-vitro % drug release graph shown below in **Figure 9**. The formulation F6 shows highest release (97.12%) within 180 seconds.

Table: 1 Selected factors and there levels (Independent variables)

S. No.	Name of factors	Levels (concentration of factor)		
		Low(-1)	Medium (0)	High (+1)
1.	X1: Concentration of HPMC (mg)	250	350	450
2.	X2: Concentration of PEG-400(ml)	0.05	0.075	0.09

Table: 2 Dependent (Response) variables

S. No.	Name of response	Unit
1.	% drug release	%
2.	Disintegration time	Second

Table: 3 Composition of Melatonin oral fast dissolving film

BATCH NO. INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
Melatonin + β-cyclodextrin solid dispersion(mg)	80	80	80	80	80	80	80	80	80
HPMC E5 (mg)	250	250	250	350	350	350	450	450	450
PEG-400(ml)	0.05	0.075	0.09	0.05	0.075	0.09	0.05	0.075	0.09
Citric acid (mg)	20	20	20	20	20	20	20	20	20
Mannitol (mg)	20	20	20	20	20	20	20	20	20
Distilled water(ml)	10	10	10	10	10	10	10	10	10

Table: 4 Absorbance data of Melatonin in ethanolic distilled water at 276.2 nm (n=3)

S. No.	Concentration (µg/ml)	Absorbance Mean± SD
1.	0	0
2.	5	0.239±0.003
3.	10	0.465±0.009
4.	15	0.659±0.006
5.	20	0.846±0.012
6	25	1.112±0.018

Table: 5 Absorbance data of Melatonin in phosphate buffer pH 6.8 at 276.2 nm (n=3)

S. No.	Concentration (µg/ml)	Absorbance Mean± SD
1.	0	0
2.	5	0.219±0.002
3.	10	0.474±0.001
4.	15	0.698±0.001
5.	20	0.885±0.004
6.	25	1.143±0.002

Table: 6 Solubility data of Melatonin in distilled water and phosphate buffer pH 6.8 (n=3)

Name of drug	Medium	
	Distilled water (mg/ml) Mean± SD	Phosphate buffer pH 6.8 (mg/ml) Mean± SD
Melatonin	0.110 ±0.002	0.538 ±0.006

Table: 7 Solubility data of solid dispersion of Melatonin in distilled water and phosphate buffer pH 6.8 (n=3)

Name of drug	Ratio	Medium	
		Distilled water (mg/ml) Mean± SD	Phosphate buffer pH 6.8 (mg/ml) Mean± SD
Melatonin+ β-cyclodextrin solid dispersion	1:1	0.936 ±0.004	8.471±0.007
	1:2	1.257±0.002	11.327±0.002
	1:3	3.632±0.003	15.136±0.006
	1:4	3.636±0.002	15.183±0.004

Table: 8 FTIR Spectra Peaks of Melatonin

Groups	Observed Value cm^{-1}	Reported Value cm^{-1}
N-H (stretch)	3300.12	3500-3300
=C-H(stretch)	2991.3	3100-3000
C-N(Amine)	1211.14	1350-1000
C=C(Aromatic)	1488.54	1600-1400
C=O(Amide)	1552.89	1700-1500
C-O-C(Ether)(stretch)	1079.59	1250-1050

Table: 9 FTIR Spectra Peaks of Melatonin and HPMC-E5

Groups	Observed Value cm^{-1}	Reported Value cm^{-1}
N-H(stretch)	3300.12	3500-3300
=C-H(stretch)	2989.96	3100-3000
C-N(amine)	1211.14	1350-1000
C=C(aromatic)	1488.54	1600-1400
C=O(amide)	1551.46	1700-1500
O-H(stretch)	3320.25	3400-3200
C-O-C(Ether)	1079.59	1250-1050

Table: 10 FTIR Spectra Peaks of Melatonin and β-cyclodextrin solid dispersion

Groups	Observed Value cm^{-1}	Reported Value cm^{-1}
N-H(stretch)	3300.12	3500-3300
=C-H(stretch)	2991.39	3100-3000
C-N	1212.57	1350-1000
C=C	1488.54	1600-1400
C=O(amide)	1554.32	1700-1500
O-H(Strech)	3320.15	3400-3200
C-O	1079.59	1250-1050
CH_2(bend)	1461.38	1480-1440

Table: 11 FTIR Spectra Peaks of HPMC-E5 with Melatonin and β-cyclodextrin solid dispersion

Groups	Observed Value cm^{-1}	Reported Value cm^{-1}
N-H(stretch)	3300.12	3500-3300
=C-H(stretch)	2989.96	3100-3000
C-N	1212.57	1350-1000
C=C	1488.54	1600-1400
C=O (amide)(stretch)	1554.32	1700-1500
C-O	1079.59	1250-1050
O-H(stretch)	3320.15	3400-3200
CH_2(bend)	1461.38	1480-1440

Table: 12 Thickness, Weight variation, Folding endurance, Drug content & Disintegration time of Formulation F1-F9.

Formulation	Thickness (mm) Mean± SD	Weight variation (mg) Mean± SD	Folding endurance (Times)	Drug Content (%) Mean± SD	Surface pH	Disintegration Time (sec) Mean± SD
F1	0.07±0.04	38.15±0.02	116	85.26±1.60	6.81	24±0.22
F2	0.08±0.07	39.38±0.11	122	91.37±1.42	6.92	18±0.36
F3	0.07±0.02	35.26±0.05	127	86.82±1.32	6.83	25±0.27
F4	0.09±0.05	36.43±0.09	134	94.21±0.52	6.76	20±0.34
F5	0.09±0.06	48.52±0.06	141	85.16±1.15	6.95	22±0.94
F6	0.08±0.02	47.35±0.04	148	97.36±1.74	6.88	15±0.40
F7	0.10±0.09	48.62±0.05	139	87.73±1.76	6.78	23±0.22
F8	0.11±0.03	49.22±0.07	144	92.82±0.68	6.69	30±0.16
F9	0.11±0.02	46.12±0.04	153	92.53±0.83	6.67	28±0.42

Table: 13 *In-vitro* % drug release data of F1 to F9 formulation of oral fast dissolving film.

S. No.	Time (in sec.)	% Drug Release data								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	0	0	0	0	0	0	0	0	0	0
2.	30	25.65± 0.13	29.14± 0.42	23.12± 0.09	25.23± 0.14	20.28± 1.24	26.56± 0.12	22.84± 0.14	24.43± 0.70	25.92± 0.06
3.	60	35.47± 1.21	36.53± 0.46	39.24± 0.33	32.27± 0.84	35.18± 1.34	38.29± 0.12	31.93± 0.24	38.85± 0.07	40.63± 0.07
4.	90	46.45± 0.23	50.17± 0.26	59.29± 0.09	49.13± 1.36	46.37± 0.07	48.31± 0.38	42.15± 0.45	45.67± 0.02	53.23± 1.24
5.	120	62.23± 2.24	67.57± 0.09	69.46± 1.39	57.34± 1.63	65.25± 0.07	66.79± 2.16	68.91± 0.72	52.82± 1.53	67.10± 1.75
6.	150	76.14± 2.02	71.69± 2.12	84.10± 0.63	80.35± 0.19	79.54± 0.78	82.15± 0.70	75.32± 0.91	67.27± 0.16	86.82± 0.02
7.	180	94.42± 0.33	92.23± 0.42	96.68±0. 32	94.43± 0.35	90.38± 0.16	97.12± 0.91	91.59± 0.53	88.47± 0.96	93.76± 0.12

Table: 14 Thickness, Weight variation, Folding endurance, Drug content & Disintegration time of optimized Formulation (F6)

Formulation	Thickness (mm) Mean±SD	Weight variation (mg) Mean±SD	Folding endurance (Times)	Drug Content (%) Mean± SD	Surface pH	Disintegration Time (sec) Mean± SD
F6	0.08±0.02	47.35±0.04	148	97.36±1.74	6.88	15±0.40

Table: 15 *In-vitro* % drug release data of optimize formulation (F6) of oral fast dissolving film.

S. no.	Time (in seconds)	*In-vitro* % drug release
		Optimized formulation F6
1.	0	0
2.	30	26.56±0.12
3.	60	38.29±0.12
4.	90	48.31±0.38
5.	120	66.79±2.16
6.	150	82.15±0.70
7.	180	97.12±0.91

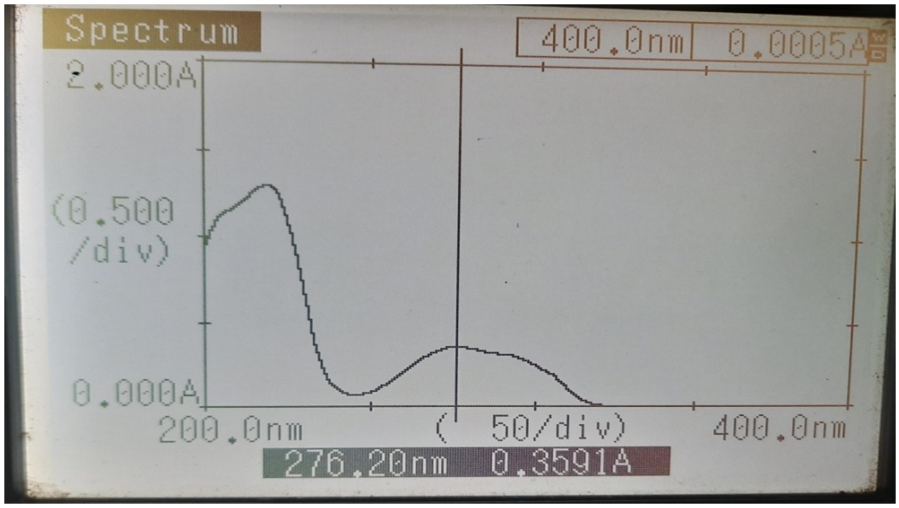

Figure 1: UV Spectrum of Melatonin

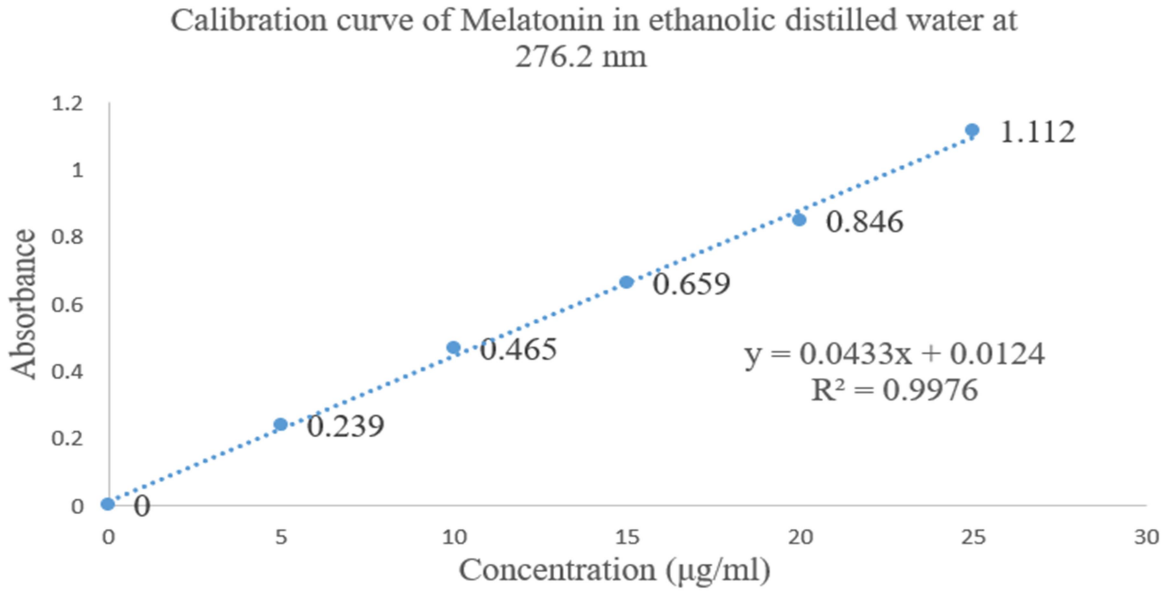

Figure 2: Calibration curve of Melatonin in ethanolic distilled water at 276.2 nm

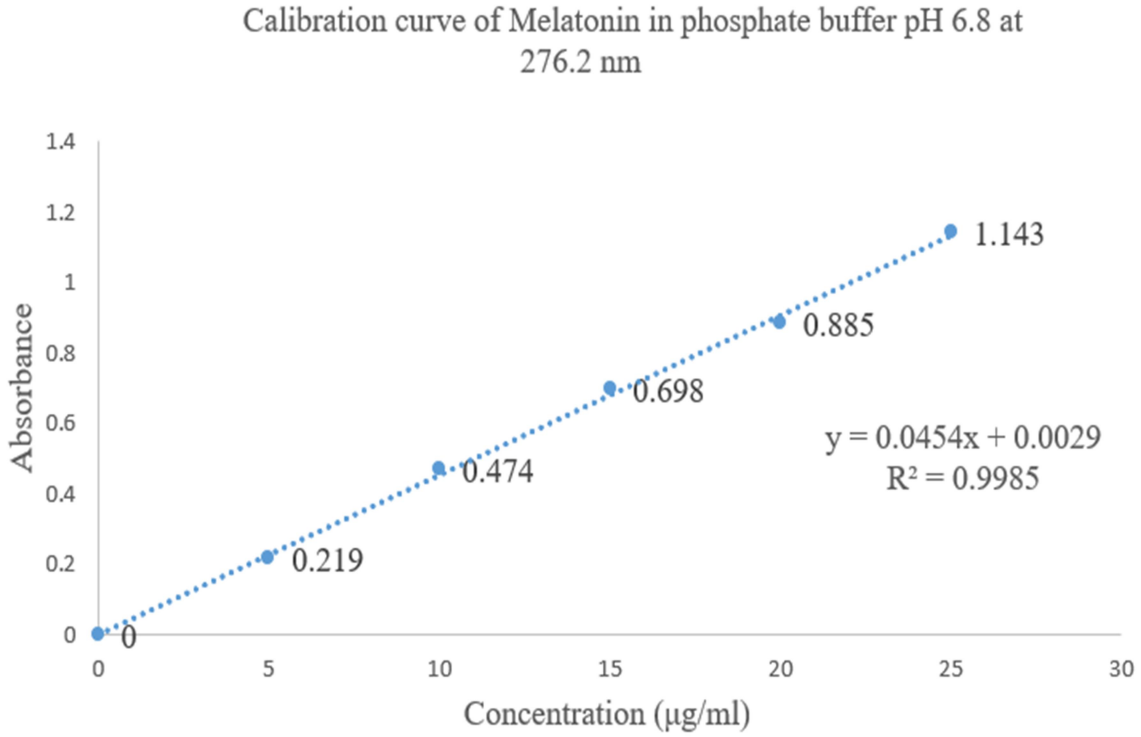

Figure 3: Calibration curve of Melatonin in phosphate buffer pH 6.8 at 276.2 nm

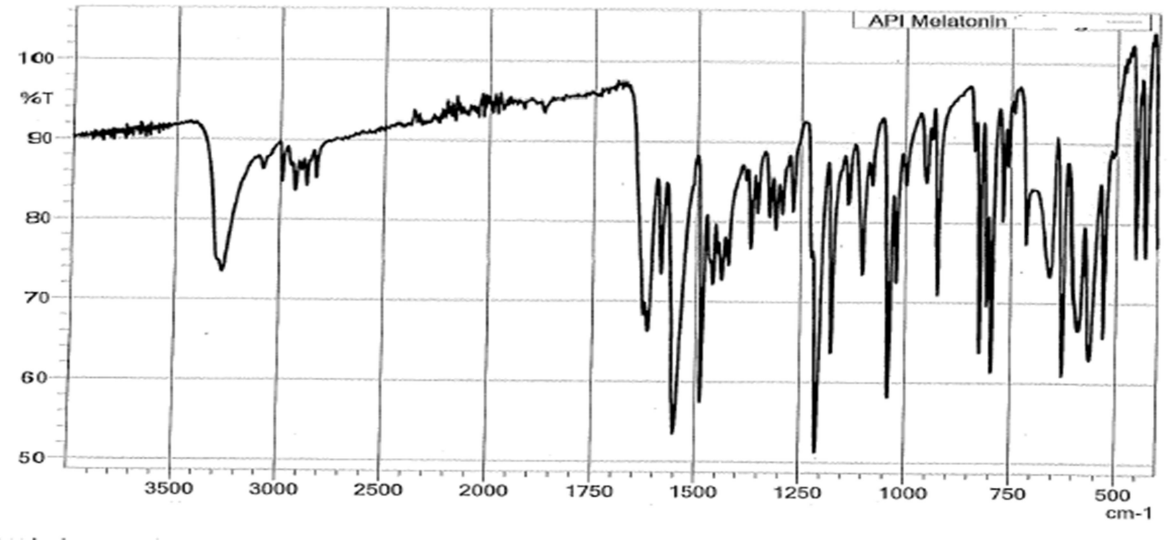

Figure 4: FTIR spectrum of Melatonin

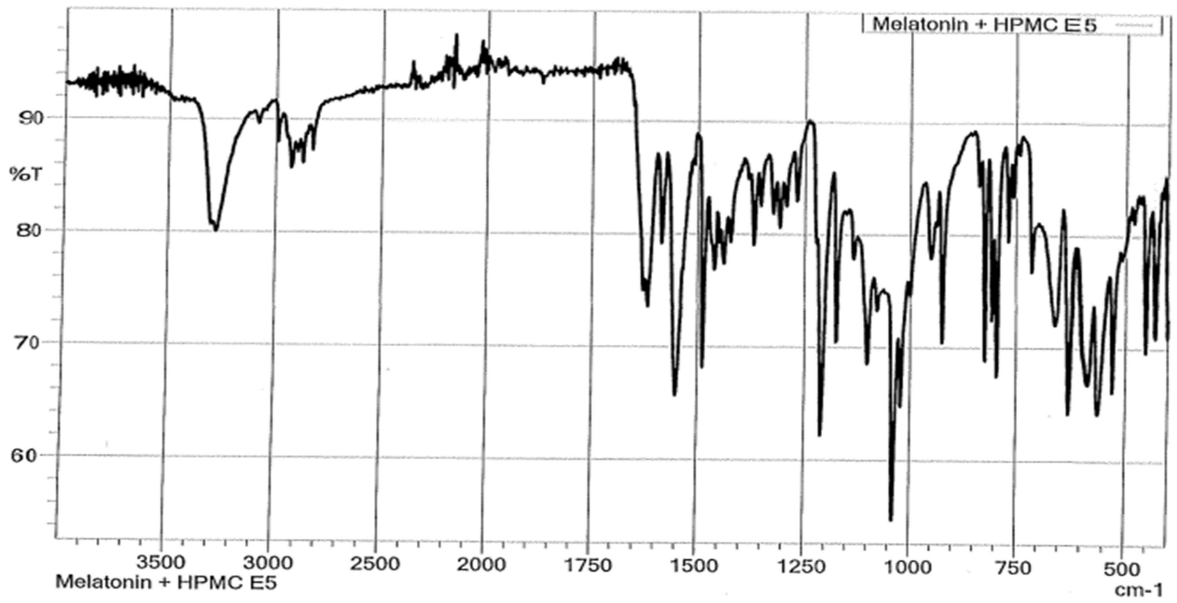

Figure 5: FTIR spectrum of physical mixture of Melatonin and HPMC-E5

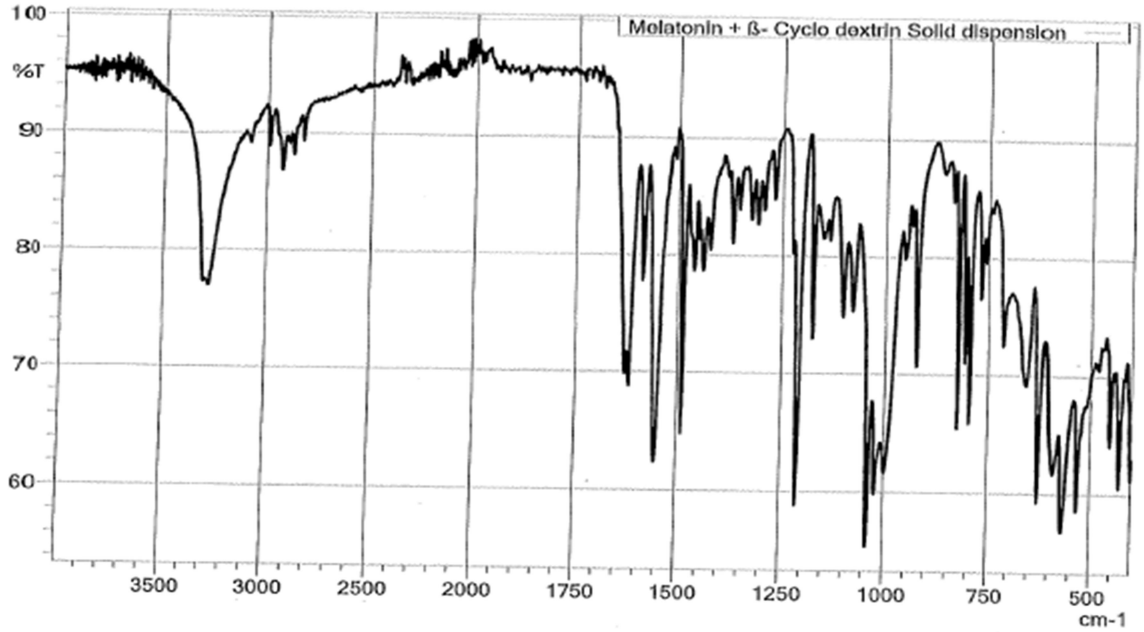

Figure 6: FTIR spectra of Melatonin and β-cyclodextrin solid dispersion

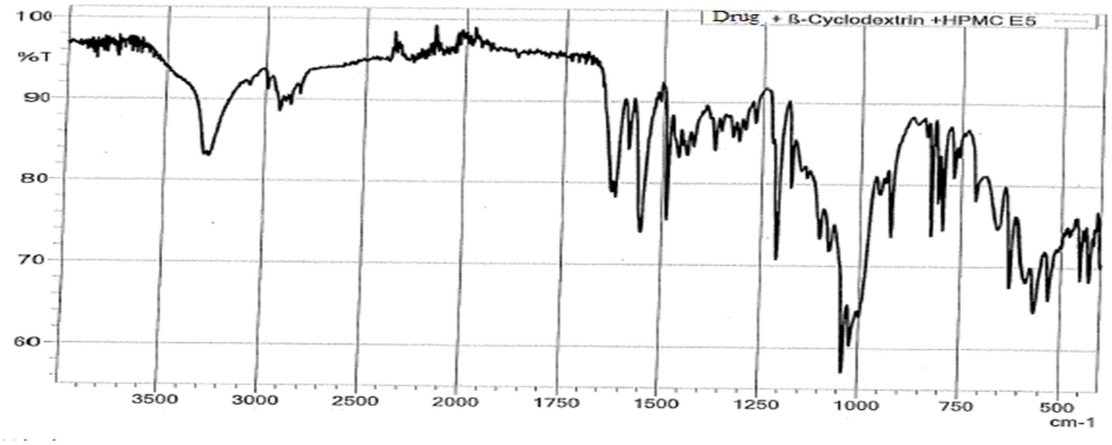

Figure 7: FTIR spectrum of HPMC-E5 with Melatonin and β-cyclodextrin solid dispersion

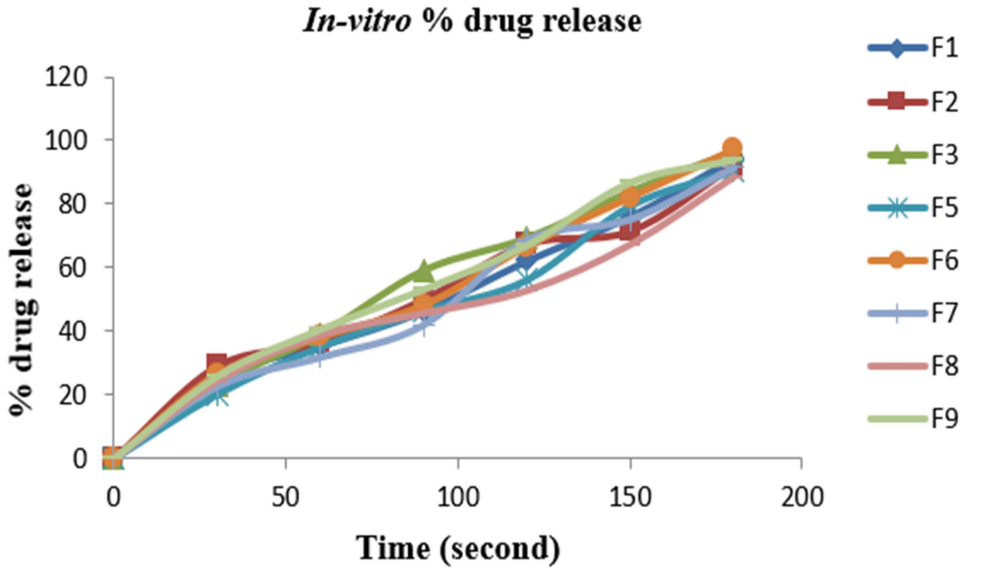

Figure 8: *In-vitro* % drug release profile of film formulations F1-F9

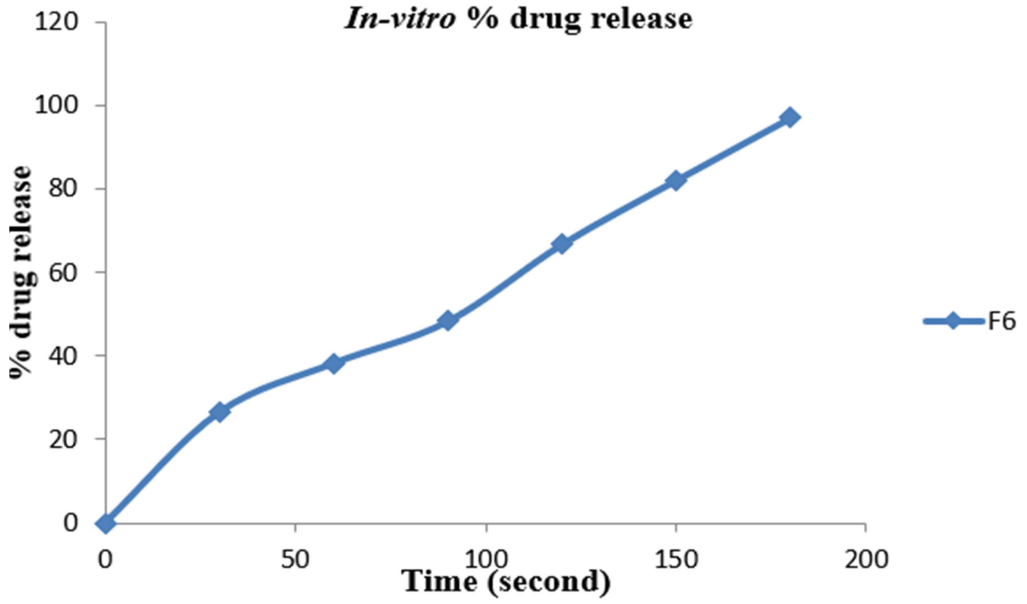

Figure: 9 *In-vitro* % drug release profile of optimized formulations F6

CONCLUSION

In the present research work an attempt has been made to optimized, formulate and evaluate oral fast dissolving film of Melatonin. In the present work solubility and bioavailability of drug was enhanced using solid dispersion. The solid dispersion of Melatonin: β-cyclodextrin was prepared in different ratio (1:1, 1:2, 1:3, 1:4) by physical mixure method. Addition of Melatonin: β-cyclodextrin solid dispersion leads to improve the dissolution characteristics and solubility of Melatonin at optimum concentration. Results revealed the maximum increase in the aqueous solubility Melatonin: β-cyclodextrin ratio of 1:3 in comparison with 1:1 & 1:2. However, SDPs had not shown any significant increase in the solubility of Melatonin on further increasing Melatonin: β-cyclodextrin ratio up to 1:4 in comparison with Melatonin: β-cyclodextrin ratio of 1:3. So, considering the above results it was found that the formulation F6 was found to be optimized formulation from the data obtained. It is observed from the formulation F6 which shown disintegration time 15 sec. and percentage cumulative drug release shown 97.12% within 180 second. Thus, it can be concluded that the drug given in the form of oral fast dissolving films should be advantageous for patients suffering from sleep disorder, avoid first pass metabolism, enhance oral bioavailability, provide fast onset of action, avoid problem of dysphasia and an effective mode of treatment.

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