FORMULATION DEVELOPMENT AND EVALUATION OF FAST DISSOLVING FILM OF TRAMADOL HCL

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***Abstract*: Oral films are an original methodology for the improvement of orally crumbling dose structures. They are thin, exquisite for all intents and purposes and can be made into different sizes and shapes like rectangular or round. The strips might be adaptable or weak, obscure or straightforward. Oral films are comprised of different hydrophilic and hydrophobic polymers to give rapid disintegration on the tongue without the requirement for water. The point of the current investigation is to foster quick dissolving films of tramadol Hydrochloride by improving drug dissolution in the oral pit. The advancement of the films diminishes the analgesic impact in less time and expands the patient's consistence. Thusly the pre-arranged films were assessed for different boundaries like physical appearance and surface of the film, thickness of the film, collapsing perseverance, moisture take-up, uniformity of weight and drug content, swelling index, in vitro disintegration considers, and in vitro dissolution contemplates. Stability studies were likewise performed. However every one of the plans similarly passed the assessment boundaries, it is presumed that oral thin films containing 400 mg of sodium alginate as the polymer in view of better dissolution profile.**

***Keywords*: Oral film, Tramadol HCL, Fast dissolving, thin film.**

INTRODUCTION:

Since the previous few decades there has been a colossal change in planning different drug conveyance frameworks to accomplish rapid beginning of activity. To beat the limits of oral dosage structures like tablets and capsules, oral thin films have been created. These are ultra thin postal stamp estimated films which are arranged utilizing hydrophilic polymers with drug and other drug excipients. This conveyance framework comprises of a thin film, which is basically positioned on the patient's tongue or mucosal tissue and quickly gets wet by salivation to break down the film rapidly. The greater part of the drug is gulped orally with the salivation and the ingestion of drug happens in the gastro-intestinal tract. These are otherwise called fast crumbling, orally deteriorating, rapidly breaking down, mouth dissolving or soften in mouth dosage structures. They offer benefits like organization without water, simplicity of gulping, rapid beginning of activity and accommodation of dosing. The quick dissolving films were arranged utilizing various sugars and flavors to work on patient consistence. Tramadol hydrochloride is a midway acting engineered narcotic analgesic restricting to explicit narcotic receptors. The principle objective of the current investigation is to foster quick dissolving oral films with rapid dissolution of drug and assimilation which might create the rapid beginning of activity[1-4].

MATERIALS AND METHODS:

Materials:

Pure drug of tramadol hydrochloride was purchased from SD Fine chemicals Pvt. Ltd., Polyethylene glycol was purchased from Feicheng Rutai Fine Chemicals CO.Ltd. Aspartame was purchased from Loba chemicals Pvt. Ltd. HPMC E-6 was purchased from SD fine chemicals Pvt. Ltd. HPMC E-15 was purchased from SD Fine chemicals Pvt. Ltd. Sodium alginate was purchased from Feicheng Rutai Fine Chemicals CO. Ltd.

Methods:

Characterization of tramadol hydrochloride

Solubility of tramadol HCL: The tramadol HCL has aqueous solubility. The solubility was obtained in distilled water and phosphate buffer pH 6.8.

Melting point determination: The melting point of tramadol hydrochloride was concluded by capillary fusion method. Fine powder of the drug was filled into a glass capillary tube which was previously sealed at one side. The capillary tube was tied to a thermometer and subjected to higher in temperatures. Therefore the temperature at which tramadol melts was confirmed[5-6].

Ultraviolet Spectroscopy: The samples were exposed to UV spectrophotometric examination and were checked for ingestion maxima (λ max) in the scope of 200 - 400 nm utilizing UV spectrophotometer in a suitable medium. The got information was contrasted and that of reference esteems in writing[7].

FTIR studies:
FTIR study was completed to genuinely look at the compatibility of drug with polymers. Infrared spectrum of tramadol not really set in stone on Fourier Transform Infrared spectrophotometer utilizing KBr dispersion technique. The baseline relationship was finished utilizing dried potassium bromide. Then, at that point the spectrum of dried combination of drug and potassium bromide was run trailed by drug with different polymers by utilizing FTIR spectrophotometer. The scope of frequency was between 400 - 4000 cm[8].

Formulation of placebo film: polymers of single or in mix were precisely gauged and disintegrated in individual dissolvable and afterward projected in a petridish with mercury as the plain surface. The films were permitted to dry for the time being at room temperature[9].

Preparation of fast dissolving oral film of tramadol hydrochloride:
Oral quick dissolving film was ready by dissolvable projecting technique. Fluid arrangement I was ready by dissolving film framing polymer, in explicit extent of refined water and permitted to mix for 3 h and saved aside for 1 h to eliminate all the entrapped air bubbles. Watery arrangement II was ready by dissolving the unadulterated drug, sugar, and plasticizer in explicit extent of refined water. The watery arrangement I and II were blended and mixed for 1 h. The arrangements were projected on to 64 cm^2 glass plate and dried in the stove at 45 ºC for 12 h. The film was painstakingly eliminated from surface of glass plate and slice as indicated by required size for testing (2 cm length, 2 cm width). The samples were put away in glass holder kept up with at a temperature of 30ºC and relative mugginess 60% ± 5% until additional investigation[10].

Table.1. Formulation of fast dissolving film of tramadol HCL (P1-P6)

Formulation code	Tramadol HCL (mg)	HPMC E-5 (mg)	HPMC E-6 (mg)	Peppermint oil (ml)	Aspartame (mg) % w/w of polymer	Poly ethylene glycol 400
P1	400	180	-	1	55	1
P2	400	280	-	1	55	1
P3	400	380	-	1	55	1
P4	400	-	180	1	55	1
P5	400	-	280	1	55	1
P6	400	-	380	1	55	1

Table.2. Formulation of fast dissolving film of tramadol HCL (P7-P12)

Formulation code	Tramadol HCL (mg)	Sodium alginate (mg)	HPMC E-15 (mg)	Peppermint oil(ml)	Aspartame % w/w of polymer	Polyethylene glycol (ml)
P7	400	180	-	1	55	1
P8	400	280	-	1	55	1
P9	400	380	-	1	55	1
P10	400	-	180	1	55	1
P11	400	-	280	1	55	1
P12	400	-	380	1	55	1

RESULT AND DISCUSSION:

Melting Point Determination: The melting point was found to be 176 ºC which corresponds to the melting point given in literature.

UV Spectroscopy : The values of correlation coefficient for the linear regression equation was obtain to be 0.998 for phosphate buffer of pH 6.8 mentioning a good positive understanding between concentration of tramadol HCL and the corresponding absorbance values.

FTIR Study:
From FTIR considers it was obviously notice that the drug has not gone through a primary modification with the polymers and other excipients utilized. Hence it was settled that in the current assessment there was no trades of the drug with the polymers or the excipients utilized.

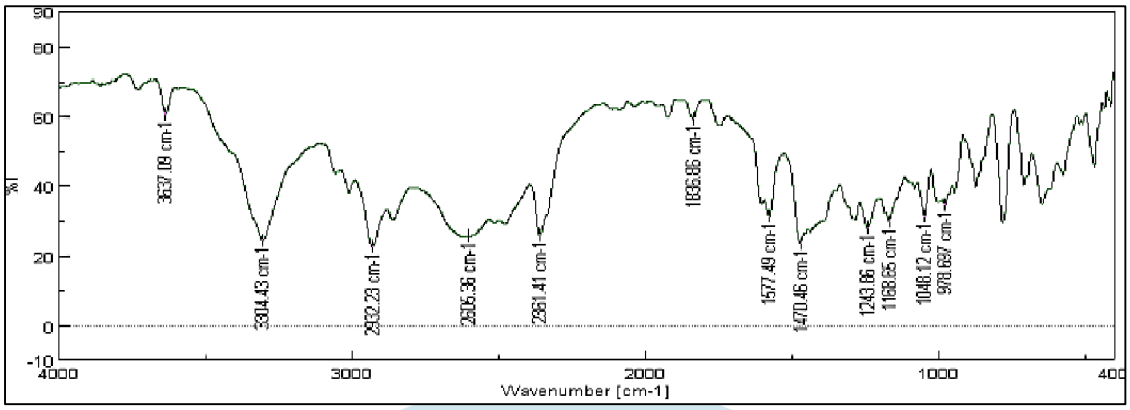

Fig.1. FTIR Spectra of pure drug Tramadol HCL

Evaluation of Fast Dissolving Films:

The tramadol HCL films were evaluated for the following properties;

Table.3. Evaluation of film for physical parameters

Formulation code	Weight (mg) ± SD, n=3	Moisture uptake	Thickness (mm) ± SD, n=3	Folding endurance ± SD, n=3
P1	55.56 ±0.05	Nil	0.9±0.04	134 ±0.43
P2	49.32 ±1.02	Nil	0.8 ±1.05	209 ±0.24
P3	51.21 ±1.34	Nil	1.1 ±0.05	145 ±0.11
P4	47.54 ±1.02	Nil	0.7 ±0.21	124 ±0.16
P5	44.43 ±0.05	Nil	0.7 ±0.54	114 ±1.01
P6	50.32 ±0.50	Nil	0.8 ±1.02	164 ±1.21
P7	46.10 ±1.21	Nil	0.9 ±0.02	148 ±0.65
P8	53.15 ±0.5	Nil	1.1 ±0.14	195 ±0.25
P9	47.88 ±1.40	Nil	0.8 ±0.53	122 ±0.43
P10	56.65 ±1.21	Nil	1.1 ±0.21	183 ±0.16
P11	55.43 ±1.50	Nil	1.1 ±0.43	172 ±0.50
P12	61.43 ±1.20	Nil	0.9 ±0.12	131 ±0.60

Table.4. Evaluation Of Films For Drug Content Uniformity, In Vitro Disintegration, Swelling Index

Formulation code	Drug content uniformity (%) ± SD, n = 3	In vitro disintegration (sec) ± SD, n = 3	Swelling index (%) ± SD, n = 3
P1	96.74 ±0.06	32 ±2.01	63.35 ±1.54
P2	91.32 ±0.05	19 ±1.50	54.34 ±2.64
P3	92.21 ±0.01	41 ±2.15	66.25 ±4.23
P4	95.32 ±0.02	22 ±1.50	57.42 ±3.54
P5	93.42 ±0.01	20 ±1.88	64.14 ±1.54
P6	91.56 ±0.03	39 ±2.02	63.24 ±4.23
P7	92.21 ±0.01	37 ±1.51	57.24 ±3.64
P8	89.32 ±0.54	47 ±2.02	64.64 ±1.54
P9	93.64 ±0.12	22 ±1.15	60.43 ±3.54
P10	88.35 ±0.02	48 ±1.11	51.54 ±2.53
P11	90.64 ±0.05	46 ±1.32	49.54 ±3.53
P12	95.65 ±0.01	20 ±1.02	56.75 ±4.53

Table.5. In Vitro Dissolution Studies Data

Time (min)	% Release											
	P1	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**	**P9**	**P10**	**P11**	**P12**
0	0	0	0	0	0	0	0	0	0	0	0	0
1	50.54	47.2	56	49.4	41	27.5	52.7	31	74.3	2.54	13.2	10.3
3	74.01	62.2	48	65.5	64	52	23.7	2.32	99.3	28	32.4	30.3
5	86.8	77.4	58	84.2	72.8	100.2	35.6	29	106.3	43	46.2	42
10	113	98.7	83	87.3	81	131	49	44.5		67	65.3	61.4
15	125	122.4	95	78.1	96.4	107	51	50.4		73	84	81
30	125	127	103	83	92.3	95	60.2	61.3		83	91	85.3
45	122	123	105	80	106	97	118	119		88	95	91.5

In Vitro Dissolution study:

Film stacked with drug identical to 25 mg of was brought into 900 ml of pH 6.8 phosphate support (dissolution medium) kept up with at 37 ± 0.5 ºC with bushel turning at 50 rpm. Tests are removed and investigated spectrophotometrically utilizing UV-Visible spectrophotometer. P9 showed 98% delivery within 3 min.

Purposes behind variances of delivery rely upon the choice of polymer, as sodium alginate is a hydrophilic polymer while HPMC (E5, E6, and E15) are hydrophobic polymers the delivery system contrasts. Sodium alginate accomplishes water to break down the drug rapidly and it gets scattered, henceforth abrupt increment of drug discharge was seen. Yet, in HPMC cases being hydrophobic the framework shaped gets so unbending and drug stays flawless within the polymer lattice. Henceforth film can't follow, hydrates, and break up rapidly to deliver the medicine for intra gastric assimilation. In this way release rate retards.

Stability Studies:

Stability studies were directed on the best delivery detailing P9. No apparent changes were seen in the items after capacity. The drug content was observed to be uniform and within the cutoff points even after capacity at (40 ºC ± 75% Rh) for 90 days, demonstrated that there were no critical changes in the drug discharge even after capacity at 40 ºC. The drug discharge qualities of the item were observed to be steady and unaltered.

Parameters	Stability data	
	Initial	3 months (40 ºC ± 75% Rh)
Thickness (mm)	0.8±0.53	0.7±0.02
Folding endurance	122±0.43	119±0.43
Drug content	93.64±0.12	93.63±0.12
In vitro disintegration (sec)	22±1.15	23
In vitro dissolution (%)	98	98

CONCLUSION:

The study of development of tramadol hydrochloride thin film revels following conclusion, as an analgesic and anti-inflammatory agent. Fast dissolving films of tramadol hydrochloride are useful due to their rapid onset of action. Fast dissolving films are a feasible alternative to the available conventional immediate release dosage forms

ACKNOWLEDGEMENT:

We are grateful to the teacher's and Principal of Loknete Dr. J. D. Pawar College Of Pharmacy, Manur, Tal. Kalwan for their helpful guidance.

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