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Design, Development and Optimization of Natural Gum Based Matrix Tablet of Tramadol Hydrochloride

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Abstract: ***The objective of this research was to develop and optimize a sustained release matrix tablet of freely soluble drug, tramadol hydrochloride using natural gums (Gumcopal and Xanthan Gum) as cheap, non-toxic, easily available polymers for matrixing. Sustained release tablet of Tramadol HCl (dose100mg) were produced by the help of wet granulation method. The prepared batches of tablets were evaluated for hardness, weight variation, friability, drug content, and in-vitro dissolution profile and found satisfactory. A3^2 full factorial design was used for optimization by taking the Gumcopal (X1) and Xanthan Gum (X2) as independent variables. Tramadol hydrochloride is a centrally acting an algesic easily available. It has dual opioid and non-opioid mechanisms of action, favorable efficacy, safety clinical profiles and non-controlled regulatory status in most markets contribute to its world wide use. A major drawback of the immediate-release formulation of tramadol four- times-a-day dosing is due to its short elimination half-life 5. 5 hr. and hence, it is necessary for the drug to develop a sustained release dosage form with reduced risk of drug administration, side effects and improved patient compliance. The formulations were found to have good pre-formulation characteristics. FTIR spectroscopy indicated the no chemical interaction within drug and excipients.***

Keywords: Tramadol hydrochloride, Gum Copal, Xanthan Gum, 3^2 full factorial design, Sustained Release Matrix, Analgesic

1. Introduction

Sustained release dosage form is widely designed for maintaining therapeutic blood or tissue levels of the drug for long period of time with minimized local or systemic adverse effects. The main advantages are economy and greater patient compliance. Sustained release dosage forms would be the most useable one for drugs having low therapeutic indices and short elimination half-lives (George et *al*., 1987) [20]. Tramadol Hydrochloride, a non-opioid and synthetic opioid of the cyclo-hexanol group, is a centrally acting analgesic with weak opioid agonist properties. The half-life of the drug is about 5. 5 hours and the usual oral dosage regimen is 50-100 mg in every 4 to 6 hrs with a maximum dosage of 400mg/day. A sustained-release formulation of tramadol is desirable to reduce the frequency of administration and to improve patient compliance. Tramado l HCL is a white or almost white, crystalline powder, freely soluble in water and in methanol, very slightly solubleinacetone.Itisacentrally-actinganalgesic1-7, used for treating moderate to moderately severe pain. The drug has a wide range of applications such as, acid reflux, treatment for restless leg syndrome, and fiber myosis.

2. Materials and method

Materials

Tramadol hydrochloride was obtained as gift sample from Shakti Bioscience (Mumbai, India). Gum Copal and Xanthan Gum obtained from Synmedic Laboratories (Faridabad, India), HPMC 15cps, Dicalcium Phosphate, Magnesium stearate were collected from Vigyankendra, Varanasi. All other chemicals and reagents used were of high analytical grade.

Method;

Drug Analysis: Tramadol hydro chloride was analyzed by UV-spectrophotometer (SHIMBADZU Japan model-1800) at 272 nm. Calibration curve was prepared in phosphate buffer of pH7. 4 in concentration ranges from 10-30mcg/ml. Correlation coefficients were found to be (r^2=0.9980) in all cases and no interference of additives used in formulation was observed.

Preparation of matrix tablet

The matrix tablet containing Tramadol Hydrochloride 100 mg were prepared by wet granulation method. The composition of tablet is shown in table 2. The powders were blended and granulated with is opropyl alcohol which is used as granulating agent. The wet mass was passed through sieve no.22# and the wet granules were dried at 50°C for 2 h. The dried granules were lubricated with magnesium stearate. The lubricated granules were compressed with a single station tablet machine.

Table 1: Formulation variable and levels

Batchcode	Variable levels incoded form	
	X1(mg)	X2(mg)
F1	-1	-1
F2	0	-1
F3	+1	-1
F4	-1	0
F5	0	0
F6	+1	0
F7	-1	+1
F8	0	+1
F9	+1	+1
Low (-1)=25 Medium (0)=37.5 High(1) =50		

Table 2: The full factorial design layout of films containing Tramadol hydrochloride;

Formulation code	Drug (mg)	Gum Copal	Xanthan Gum	HPMC 15cps	Dicalcium Phosphate (mg)	Magnesium stearate (mg)
F1	100	25	25	30	65	5
F2	100	37.5	25	30	52.5	5
F3	100	50	25	30	40	5
F4	100	25	37.5	30	52.5	5
F5	100	37.5	37.5	30	40	5
F6	100	50	37.5	30	27.5	5
F7	100	25	50	30	40	5
F8	100	37.5	50	30	27.5	5
F9	100	50	50	30	15	5

Where**, X1** indicates Gum Copal and **X2** Xanthan Gum.

Evaluation of granules;

The flow properties of granules were determined by different parameters like angle of repose (Θ) of granules was determined by the funnel method. Angle of repose was calculated by using the equation,

$$\tan \Theta = \frac{h}{r},$$

where h and r are the height and radius of the pile respectively. Both bulk density (BD) and Tapped density (TD) were determined and calculated by using following equation, BD = weight of granules/ bulk volume , TD = weight of granules/ tapped volume. The compressibility index of the granules was determined by Carr's index using equation, Carr's index = [(TD- BD) X 100)]/TD. All values were found to be satisfactory (**table 3**).

Evaluation of tablets

Weight Variation

For weight variation test, 20 tablets were randomly selected and individually weighed. The average weight and weight variation in the form of standard deviation of 20 tablets was calculated.

Friability: 10 tables were weighed and placed in Roche's friabilator (Synmedic lab., Faridabad) and apparatus was rotated at 25 rpm for 4 minutes. The percentage friability was measured using the formula,

% F = { 1- (Wt/W)} x 100…….(1)

Where %F= friability in percentage

W = Initial weight of tablet

Wt = weight of tablet after revolution

Hardness: Hardness was measured using Monsanto hardness tester. For each batches 10 tablets were tested.

Dimension: Twenty tables were randomly selected from each batch and there thickness and diameter were measured by using digital vernier callipers.

Drug Content of Tramadol HCL

Precisely weigh of 100 mg of Tramadol HCl reference Standard into a 100 ml volumetric flask, dissolve in methanol and dilute to volume. Precisely weigh an amount of tablet powder, equal to 100 mg of Tramadol HCl, into 100.0 ml volumetric flask, and add methanol to volume. Stirr during one night to allow tramadol to dissolve. Centrifuge and inject (20 µl) the clear solution and % drug content of the filtrate was recoded at λmax of 272 nm with help of UV spectrophotometer. [7]

In-vitro dissolution study

Conducted in-vitro drug release study of prepared matrix tablets for a period of 10 hrs. using a 6 station USP TDL-06L (Synmedic lab., Faridabad) apparatus at 37±0.5^{0}C and at 50 rpm speed, the in vitro release study was performed in 0.1 N HCL pH 1.2 for 2 hrs and in phosphate buffer pH 7.4 up to 10 hrs. At each interval 5 ml of sample was withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After proper dilution and filtration, the sample solutions were analyzed at 272 nm for tramadol hydrochloride by UV-Visible spectrophotometer. The amount of drug present in the samples was calculated. Some marketed sustained release (CSR tablet: TRAMACON®, TRAMAL® was purchased from the market and was evaluated for *in vitro* release characteristics following the above procedure.

Optimization of variables using full factorial Design

A 32 randomized full factorial design was used in present study. Two factors were evaluated in this design, each at three levels, and experimental trials were performed for all nine possible combinations. The amount of Gum Copal (X1) and Xanthan Gum (X2) were chosen as independent variables in 32 full factorial designs. The formulation layout for factorial design batches (F1-F9) is shown in Table 1. The prepared formulations were evaluated for drug content; drug release and hardness were selected as dependent variables. In addition the individual dependent variables (Drug content, drug release and hardness) were calculated with help of Design Expert 8.0.6.1 trial software and applied to approximate surface response, contour plots and correlation between actual and predicted values. The general model as shown below was generated,

$$Y = b0+b1x1+b2x2+b3x1x2+b4x1 +b5x2 +b7x1x_2 \ldots (2)$$

Where Y is the dependent variable, b0 is the arithmetic mean response of all 9 batches. The main effects (X1 and X2) represent the average result of changing one factor at a time from its low to high value. When two factors are simultaneously changed, it shows how the response changes in the interaction terms (X1, X2). The polynomial terms (X12andX22) are included to investigate nonlinearity. [0]

Compatibility study;

Fourier Transform Infrared Spectroscopy;

Drug polymer interactions were studied by FTIR spectroscopy. The spectra were recorded for pure drug and physical mixture of polymers with API using JASCOFT/IR-4200, JASCO. The samples were prepared as KBr discs. The scanning range was 400-4000 cm-1 and resolution was 2 cm-1.

Thermal analysis;

Differential scanning calorimeter (DSC) was carried out

using DSC-60, SHIMADZU. The sample were hermetically sealed in aluminium pans and heated over the temperature range 25oC to 300oC with heating rate of 10oC/min.

X-ray diffraction studies;
The crystallite of tramadol hydrochloride was studied by X-ray diffractometry, before and after tablet formulation. The instrument was set up with the tube voltage of 40 kV, current 30 mA and scanning rate of 50/min, over a range of 8-600 diffraction angle (2Ɵ) range.

Kinetic Study
Different kinetic equations [zero order (Eq.3), first order (Eq.4) and Higuchi's equation (Eq.5)] were applied to interpret the release rate of drug from the matrix system. Coefficient of correlation (r) value was used for the selection of most appropriate model.

$$Mt = M0 + k0t \quad \text{(3)}$$
$$\text{In } Mt = \text{In } M0 + k1t \quad \text{(4)}$$
$$Mt = M0 + kHt1/2 \quad \text{(5)}$$

Where Mt is cumulative amount of the drug released at any time, t, and M0 is dose of the drug incorporated in delivery system. K0, k1 and kH are rate constants for zero order, first order and Higuchi models respectively. According to dissolution data exponential Korsmeyer-Peppas equation were fitted which is suitably used to describe and analyse the drug release behavior from the polymeric systems. [12]

$$Mt/M\infty = Ktn \quad \text{(6)}$$

Mt/M∞ is the fraction of drug release at time t, and K is the kinetic constant, n is the release exponent indicating the mechanism of drug release, K was a constant which incorporates the properties of the macromolecular polymeric system and drug and n was the diffusional exponent, which characterized the drug transport mechanism (Agarwal and Mishra., 1999). When, n < 0.5 indicates fickian diffusion, when n ≥0.500 to 0.890 indicates non-fickian or anomalous diffusion, when n=0.890 case II transparent, n > 0.89 indicates super case II transport.[6]

Dissolution profiles were compared for selection of optimum batch
The similarity factor (f2) given by SUPAC guidelines for a modified release dosage form was used as a basis to compare dissolution profiles. The dissolution profiles are considered to be similar when f2 is between 50 and 100. The dissolution profile of products were compared using a f2 which is calculated from following formula,

$$f2 = 50 \bullet \log \{[1+(1/n)\Sigma t=1n (Rt - Tt)2] -0.5 \bullet 100\} \quad \text{(7)}$$

Where *n* is the number of time points, R is the dissolution value of the reference at time t, and T is the dissolution value of the test at time t. [16]

3. Result and Discussion

The matrix tablet containing Tramadol hydrochloride were designed with the objective of sustained release drug delivery for improving bioavailability and patient compliance by reducing multiple dosing and hence reduces side effect. The hydrophobic natural gums i.e. Gum copal and Xanthan Gum were selected for preparation of sustained release matrix tablet. The prepared tablets were found to be good without any tablet defects i.e. sticking, chipping, capping to be satisfactory.

Optimization of different formulations:
The Model F-value of 873.97 implies the model is significant**.** There is only a 0.01% chance that a "Model F-Value" this large could occur due to noise. In this optimization case study A, B, B2 are significant model terms. The "Pred R-Squared" of 0.9916 is in reasonable agreement with the "Adj R-Squared" of 0.9981. "Adeq Precision" measures the signal to noise ratio. A ratio greater than 4 is desirable and ratio of 84.705 indicates an adequate signal. Final models in terms of coded factors for drug content was as follow, table

Drug release = 80.28-1.94X1-4.84X2+0.30X1X2-0.37X 2+1.39X 2

The calculated R-sqeared, Adj R-squared, Pred R-squared and Adeq Precision value for dug content were 0.9993, 0.9981, 0.9916 and 84.705 respectively. The Model F- value of 873.96 implies the model is significant. As regards the effect of gum concentration, decrease in drug release rate was observed when gum copal and Xanthan Gum content in the matrix was increased. This may be due to the higher concentration of gums in tablet might have produce dense matrix around the drug particles, which providing more barriers for them to scape and dissolve. Further, these dense matrix, especially when it hydrophilic in nature, may be expected to favour less penetration of dissolution medium in the tablets. This may also be the auxiliary reason for obtaining slow drug release profile through gum copal and Xanthan Gum matrix tablets.

Table 3: Response 1-Drug release; Analysis of variance (ANOVA) for selected factorial model

Source	Sum of square	D f	Mean square	F value	p-value Prob>f	
Model	167.15	5	33.43	873.97	<0.0001	Significant
A-Gum Copal	22.27	1	22.27	582.27	0.0002	
B-Xanthan Gum	140.36	1	140.36	3669.27	<0.0001	
AB	0.37	1	0.37	9.57	0.0537	
A2	0.27	1	0.27	7.03	0.0536	
B2	3.88	1	3.88	101.51	0.0021	
Residual	0.11	3	0.038			
Core total	167.26	8				

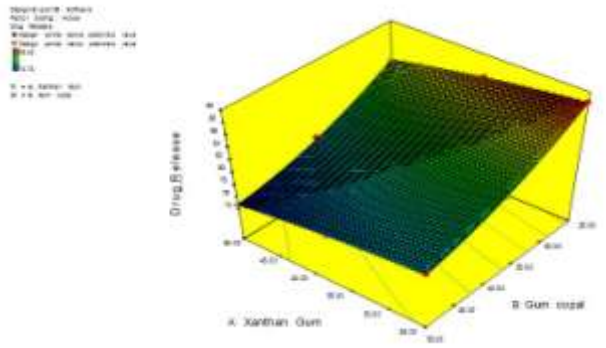


Figure 1: Surface response plot for drug release;

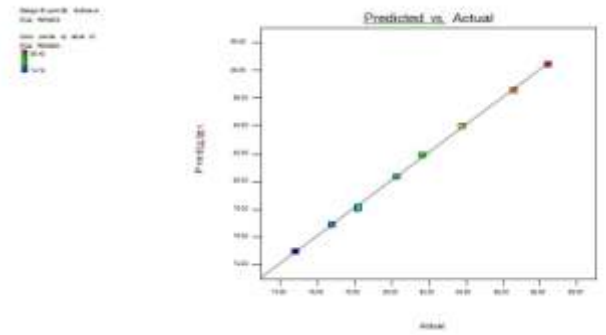


Figure 2: Correlation between the actual value and predicted value;

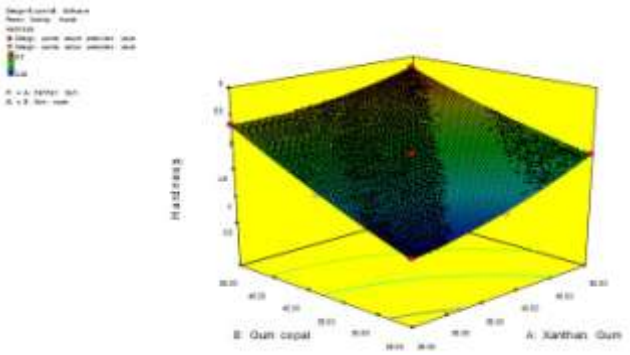


Figure 3: Contour plot between Gum Copal and Xanthan Gum for drug content

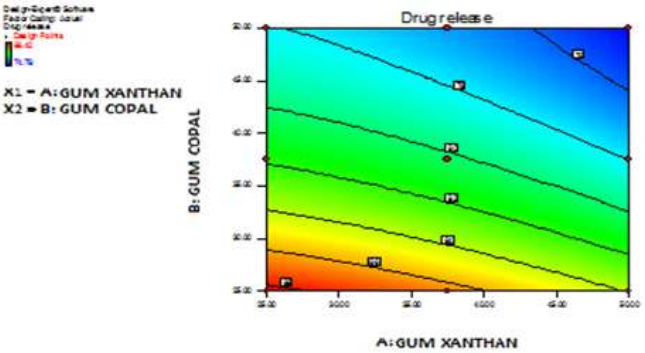


Figure 4: Surface response plot for Hardness

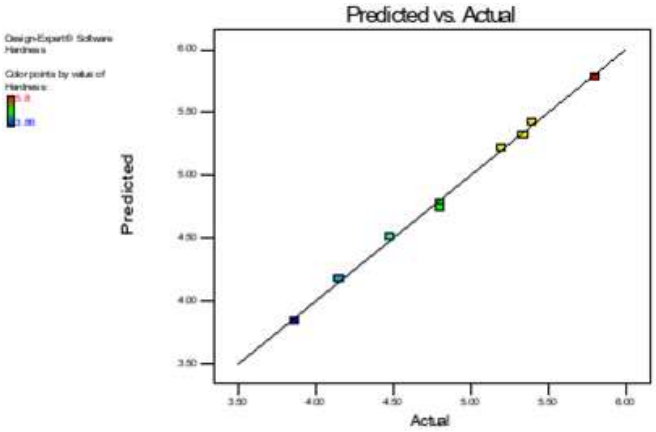


Figure 5: Correlation between the actual value and predicted value;

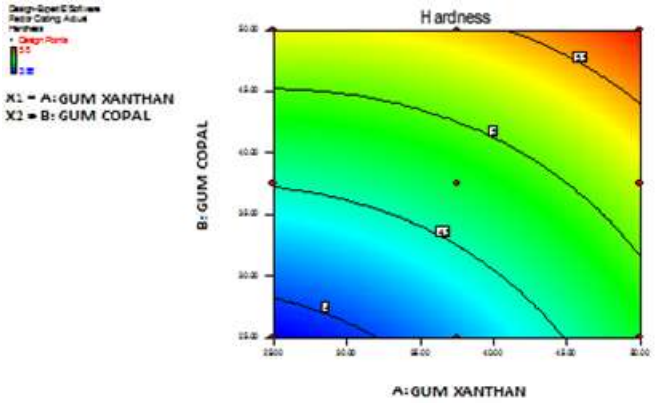


Figure 6: Contour plot between Gum Copal and Xanthan Gum for Hardness;

FTIR Spectroscopy; The IR spectra of pure drug tramadol hydrochloride and optimized product have been showed in (fig10 a and b) respectively. The major peaks observed in the spectra for tablet formulation were OH-stretching at 3650-3700 cm-1, C-H stretching at 3400-3000 cm-1 (methoxy group), C-H stretching at 3000-2900cm-1 (methyl group), C=ring stretch at 1500-1600 cm-1, C-N stretch at 1300-1250 cm-1,C- O-C asymmetric stretch at 1190-1160 cm-1, C-H bend at 790-750 cm-1, C==C bend at 700-690 cm-1, which are characteristics of tramadol hydrochloride. When this is compared to IR spectra of physical mixture, it was nonobious interaction between drug and the polymers.

Table 5: Characteristics peaks for IR spectra

Characteristics Peak	Functional Groups	Peak (cm-1)
C-N stretching	C-N group	1300-1250 cm-1
C-H stretching	0CH3 group	3400-3000cm-1
C-H Stretching	CH3 group	3000-2900 cm-1
C=C bending	C=Cinsix member ring	700-690 cm-1
=C-Houtofplane bending	C=Caromatic group	790-750 cm-1
C=ring stretching	C=ring	1500-1600 cm-1
O-H stretching vibration, inter-molecular hydrogen bonding	Bonded with–OH	3650-3700 cm-1

(c)- Tramadol hydrochloride

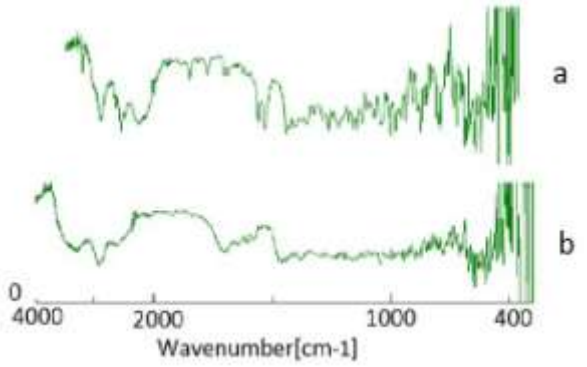
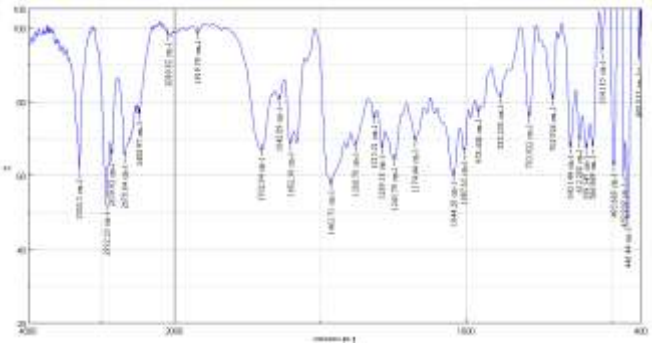


Figure 7: Ir spectra of, (a)-pure drug Tramadol hydrochloride, (b)- physical mixture



F9

Figure 8: IR spectra of optimized product

Differential Scanning Calorimetry

In order to confirm the physical state of the pure drug, DSC of the drug alone, physical mixture of drug and the optimized product. The DSC trace of drug showed a sharp endothermic peak at 182.21°C, its melting point. The physical mixture of drug and polymers showed the endothermic peak at 176.8°C as the individual component, indicating that there was no interaction between the drug and the polymer in the solid state.

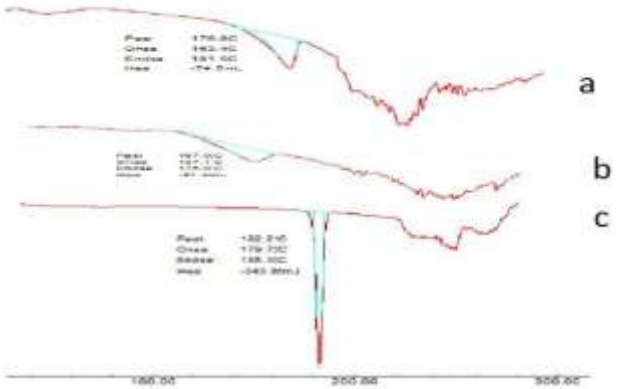


Figure 9: DSC (a)-physical mixture,(b)- optimized product,

X-Ray Diffractogram

The X-ray diffractograms of Tramadol HCl confirmed its crystalline nature (fig…), as evidenced from the number of sharp and intense peaks which are absent in case of amorphous drugs. The pure Tramadol Hydrochloride exhibited the diffraction at 2Θ values of 10.670, 13.680,18.780, 21.670, 24.690, 26.390, 29.750, 31.020, 42.180. The X- ray diffractogram of tramadol hydrochloride confirm its crystalline nature, as evidenced from the appearance of number of sharp and intense peaks. However, finally the diffraction pattern of optimized product represents complete appearance of sharp and intense peaks which indicates that the drug till in its crystaline nature and there is no inhibitory effect of selected polymers on the crystallization of drug, which indicate there is no changes in the molecular mobility of drugs and hence confirms its crystalline nature.

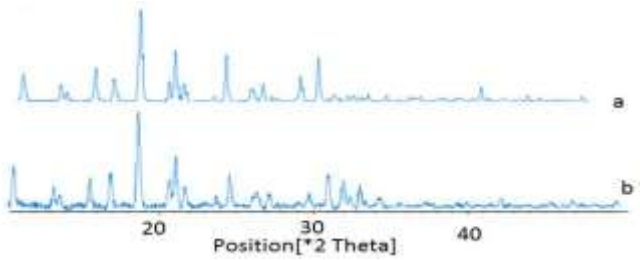


Figure 10: x-ray diffractrogram of (a)-Tramadol hydrochloride, (b)-optimized product F9

Evaluation of granules

The physical mixture for matrix tablets were characterized with respect to angle of repose, bulk density, tapped density and Carr's index (table 6). Angle of repose were found between 25 o -31o and Carr's index values were found between 12-18 % for the powder of all the batches indicating excellent to poor flow ability and compressibility. Hausner's ratio was found to be between 1.14 to1.23 for all the batches indicating that passable to poor flow properties.

Table 6: Pre-compression evaluation matrix tablets of Tramadol Hydrochloride

Formulation	Angle of repose (o)	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Hausner's ratio
F1	25.79±0.15	0.241±0.010	0.285±0.05	17.52±0.07	1.22±0.03
F2	31.27±0.46	0.322±0.010	0.374±0.07	12.56±0.52	1.14±0.01
F3	26.91±0.33	0.283±0.00	0.352±0.08	18.05±0.71	1.21±0.02
F4	27.51±0.04	0.294±0.00	0.366±0.06	18.37±0.35	1.22±0.01
F5	25.36±0.18	0.296±0.00	0.362±0.01	15.14±0.25	1.19±0.03
F6	26.59±0.04	0.278±0.00	0.331±0.00	15.17±0.05	1.16±0.07
F7	29.11±0.13	0.292±0.00	0.344±0.09	16.43±0.25	1.17±0.05
F8	26.99±0.11	0.285±0.01	0.347±0.06	16.92±0.12	1.21±0.03
F9	28.41±0.16	0.289±0.00	0.338±0.06	16.09±0.03	1.23±0.04

Drug Content and Physical Properties

Prepared tablets were evaluated for parametric tests (Table7). The drug content in various formulations was varied between 97.83±0.67 to 102.1±0.88%.

The Maximum thickness and hardness of prepared tablets were found between 3.51± 0.019mm and 5.80kg/cm2 respectively. Friability of prepared tablets ranges between 0.466± 0.016 to .913±0.020.

Table 7: Characterization of prepared tramadol hydrochloride matrix tablet (100mg):

Formulation	Wt variation (mg)	Hardness (kg/cm2)	Friability (%)	Thickness (mm)	Drug content (%)
F1	5.753±0.32	3.86±0.030	0.746±0.015	3.313±0.030	100.4±0.50
F2	6.323±0.09	4.15±0.025	0.663±0.015	3.320±0.095	102.1±0.88
F3	5.880±0.21	4.80±0.050	0.786±0.030	3.493±0.025	101.1±0.90
F4	5.873±0.08	4.50±0.015	0.913±0.020	3.396±0.020	98.67±0.46
F5	6.963±0.13	4.80±0.015	0.676±0.015	3.370±0.020	99.48±0.42
F6	5.530±0.25	5.20±0.026	0.760±0.030	3.363±0.025	97.83±0.67
F7	5.130±0.18	5.340±0.019	0.666±0.013	3.510±0.019	100.7±0.52
F8	4.540±0.27	5.40±0.026	0.566±0.015	3.510±0.029	99.94±0.57
F9	5.296±0.13	5.80±0.025	0.466±0.016	3.486±0.030	98.78±0.38

Invitro Drug release study

The drug release data are shown in (table 8 and fig 11) drug release from the tablets prepared by wet granulation were found 88.42%, 80.25%, 78.21%, 76.78% and 74.78% for F1, F5, F7, F8 and F9 respectively after 10 hr. Different combinations of natural gums (copal and xanthan) with HPMC and as triple mixture of these polymers were used to provide matrix tablets for sustained release of water-soluble tramadol HCl. In the different formulation it was observed even the concentration of using gums were low (F1), the release of drug have shown about 88.42 % after 10 hr. But as the ratio of the gums varies results were varied accordingly. The formulation F9 contained maximum concentration of both natural gum which reflect the more effective release retardant (74.78%) as compare to others one.

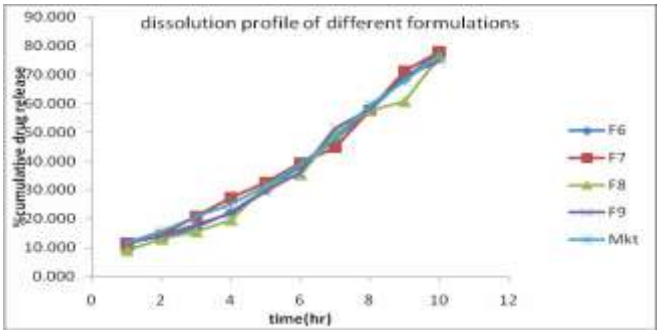


Figure 12: In vitro dissolution profile of prepared formulations (F7-F9, Mkt)

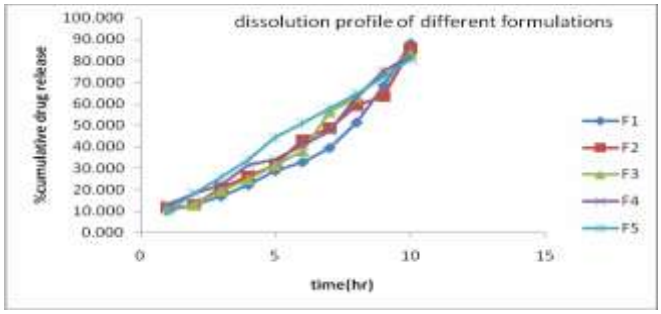


Figure 11: In vitro dissolution profile of prepared formulations (F1-F6)

Table 8: Regression coefficient of different formulations

Formulation	Cumulative% drug relase (after 10hr)	Kinetic release model for dissolution data				
		Zero order (R2)	First order (R2)	Higuchi plot (R2)	Hixon crowell (R2)	Korsmeyer Peppas (R2)
F1	88.42	0.964	0.847	0.815	0.778	0.910
F2	86.59	0.960	0.891	0.897	0.919	0.941
F3	83.78	0.965	0.884	0.898	0.921	0.927
F4	81.67	0.963	0.869	0.900	0.933	0.949
F5	80.25	0.998	0.960	0.983	0.987	0.991
F6	78.18	0.974	0.897	0.909	0.930	0.956
F7	78.21	0.969	0.888	0.906	0.917	0.952
F8	76.78	0.967	0.951	0.905	0.928	0.940
F9	74.78	0.963	0.910	0.895	0.932	0.917

Drug release kinetics;

In order to investigate the drug release kinetics, data were fitted to models (Sankar *et al*., 2001) representing zero-order and Korsemayer-Peppas model. The data were analysed by the regression coefficient method and regression coefficient value (r2– value) of all batches were shown in Table 9 and 10.

On analysing regression coefficient values of all batches, it was found that all Batches followed zero order and Korsemayer-Peppas model. The values of *n* were in the range of 0.359 to 0.556 (i.e. more than 0.5, table 9) indicating Non-Fickian release (diffusion controlled), which indicated drug release to occur through diffusion and relaxation.[20]

Table 9: Kinetic Treatment for dissolution data

Release Model	Parameter	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Zero order	Slope(b)	8.550	7.832	8.479	7.767	7.818	7.859	7.510	7.550	7.566
	Intercept(a)	-5.280	-2.756	-5.019	-0.011	3.021	-5.155	-1.524	-4.662	-3.171
	R^2	**0.964**	**0.960**	**0.965**	**0.963**	**0.998**	**0.974**	**0.969**	**0.967**	**0.963**
First order	Slope(b)	-0.058	-0.062	-0.077	-0.071	-0.070	-0.064	-0.063	-0.053	-0.061
	Intercept(a)	2.096	2.087	2.137	2.104	2.075	2.108	2.091	2.076	2.091
	R^2	**0.847**	**0.891**	**0.884**	**0.869**	**0.960**	**0.897**	**0.888**	**0.951**	**0.910**
Higuchi plot	Slope(b)	32.38	32.35	34.96	32.09	33.15	32.44	31.04	31.21	31.17
	Intercept(a)	-35.63	-32.37	-36.92	-29.38	-28.47	-34.83	-29.97	-33.27	-31.60
	R^2	**0.815**	**0.897**	**0.898**	**0.900**	**0.983**	**0.909**	**0.906**	**0.905**	**0.895**
Hixon-crowell	Slope(b)	-0.200	-0.179	-0.210	-0.202	-0.191	-0.183	-0.18	-0.171	-0.175
	Intercept(a)	4.976	4.835	4.937	4.841	4.755	4.892	4.836	4.862	4.846
	R^2	**0.778**	**0.919**	**0.921**	**0.933**	**0.987**	**0.930**	**0.917**	**0.928**	**0.932**
Korsme-yerpeppas	Slope(b)	0.918	0.897	0.936	0.819	0.930	0.980	0.866	0.970	0.881
	Intercept(a)	0.873	0.935	0.914	1.094	0.992	0.843	0.956	0.835	0.924
	R^2	**0.910**	**0.941**	**0.927**	**0.949**	**0.991**	**0.956**	**0.952**	**0.940**	**0.917**
	N	**0.503**	**0.459**	**0.477**	**0.483**	**0.359**	**0.498**	**0.502**	**0.497**	**0.556**

4. Conclusion

It can be concluded from above study that, the matrix tablets containing tramadol hydrochloride using different ratio of hydrophobic natural gums (gum copal and Xanthan Gum) were prepared by wet granulation method were found to be good without any tablet defects i.e. sticking, chipping, capping. Natural gums (gum copal and Xanthan Gum) were used in the as 10%, 15% and 20% (w/w) of total tablet weight with the combination of HPMC 15cps. Both gums with 20% concentration retarded the tramadol hydrochloride release beyond 10 hr. Gum copal was found more effective than Xanthan Gum at low concentration (10%) with combination of HPMC 15cps in sustaining the drug release rates. The prepared formulations were followed the zero order release kinetics. Gum copal and Xanthan Gum was not effective separately with combination of HPMC 15cps. Formulation (F9) containing both gums (gum copal and Xanthan Gum 0f 20% w/w) with HPMC 15cps shows greater release retarded batch.

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