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Formulation and evaluation of tramadol hydrochloride floating tablets by using different polymers

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ABSTRACT

The gastric emptying time and the variation in pH in different segments of gastrointestinal tract (GIT) are the major challenging task for the development of oral controlled release drug delivery system. Various attempts have been made to enhance the residence time of the dosage form within the stomach. Gastro retentive system can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of the drug in the GIT. Potential drug candidates for gastro retentive drug delivery system (GRDDS) are drugs, which are locally active in the stomach eg. Misoprostol, antacids etc., and drugs that have narrow absorption window in GIT eg. L-DOPA, para amino, benzoic acid etc. In addition drugs which are unstable in the intestinal or colonic environment like captopril and metronidazole. It has been suggested that prolonged local availability of antimicrobial agents may augment their effectiveness in treating H. pylori related peptic ulcer. Moreover, it has been reported that bactericidal effect of clarithromycin and garcinol are time and concentration dependent. GRDDS however, are not suitable for drugs that may cause gastric lesions eg. Non-steroidal anti inflammatory drugs.

AIM AND OBJECTIVES

Formulation and evaluation of tramadol hydrochloride floating tablets by using different polymers

OBJECTIVES

- The Gastro retentive drug delivery tablets prepared by using direct compression method.
- To release the drug upto longer period of time
- To maximize the bio availability of a drug
- To eliminating the side effects and minimising the dose dumping and minimise the adverse effects.
- To study the kinetic modelling.
- To perform stability study for selected formulation

PLAN OF WORK

- Literature Survey; the various work carried out on this topic is reviewed.

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- Procurement of drug, polymer and other ingredients required for the study.

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- Physical characterization of drug sample including Description, Melting point, Solubility and Drug –excipient compatibility studies.

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- Formulation of tablets by using direct compression method.

⇩

- Evaluation of tablets.

⇩

  - Pre compression parameters:
  - Bulk density
  - Tap density
  - Angle of repose
  - Compressibility index
  - Hausners ratio
- Post compression parameters:

⇩

  - Weight variation
  - Friability
  - Disintegration
  - Hardness
  - Drug content estimation
- To study Invitro Dissolution Profile.
- To perfume Stability Study of selected formulation .

METHODOLOGY, MATERIALS AND METHOD

Table 1: Formulation table of tramadol hcl floating tablets

Ingridients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Tramadol hcl	40	40	40	40	40	40	40	40	40
HPMCK4M	20	-	30	-	40	-	20	40	30
Xanthin	-	20	-	30	-	40	20	40	30
NAHCO3	10	10	10	10	10	10	10	10	10
MCC	127	127	117	117	107	107	107	66	87
Mg.stearate	2	2	2	2	2	2	2	2	2
Talc	1	1	1	1	1	1	1	1	1
Total wt	200	200	200	200	200	200	200	200	200

RESULTS

Solubility studies

Solubility of the TRAMADOL in various solvents

Table. No: 2 Table showing solubility studies of the active pharmaceutical ingredient

Calibration curve of the TRAMADOL 0.1N HCL

Solvent	Solubility properties of drug (1gm)
Water	Readily Soluble
Ethanol	Freely Soluble
Methanol	Freely Soluble
Ether	Insoluble

Table. No: 3 Table showing values of the calibration studies in 0.1 Normal HCL buffer solution

Concentration (µg/ml)	Absorbance
0	0
2	0.242
4	0.53
6	0.762
8	0.98
10	1.24

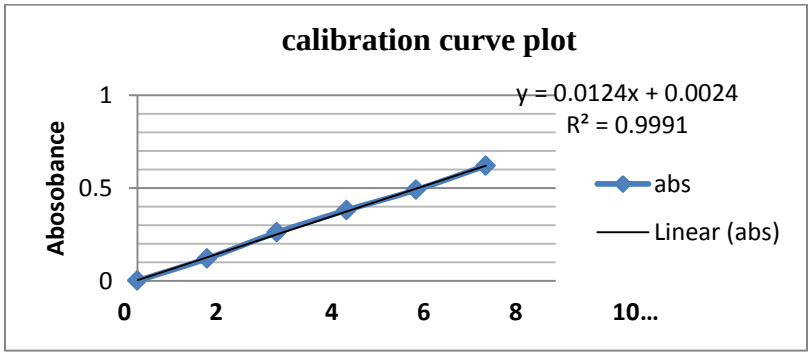


Fig. No 1: Picture showing standard

FTIR STUDIES

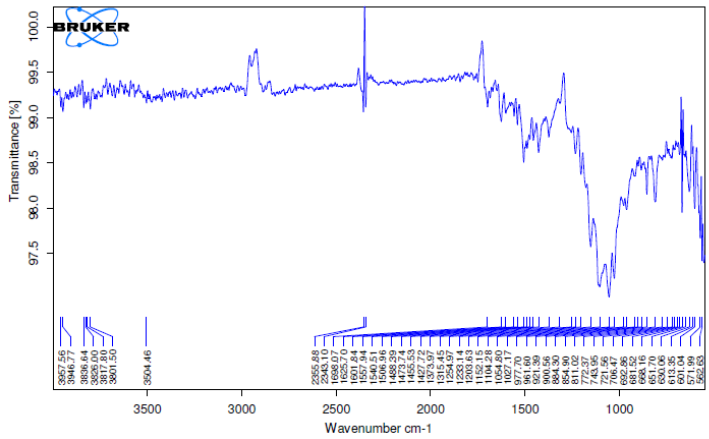


Fig. No: 2 FTIR Spectra of the pure drug tramadol hcl

Table. No: 4 Showing spectra of pure drug substance stretch bonds values

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	3600-3500	3500.92
2	OH Bending	1100-1070	1084.03
3	C-H stretching	3200-3100	3095.95
4	C-N stretching	1350-1100	1105.25

Table. No: 5 The table showing pre-compression values of the F1-F5

Pre-compression parameters of the F1-F5:

Formulation	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	22.38±0.13	0.32±0.02	0.42±0.02	16.78±0.13	1.25±0.01
F2	23.52±0.28	0.33 ±0.02	0.46±0.04	17.8±0.04 1.	1.24±0.01
F3	23.19±0.19	0.33±0.00	0.44±0.01	16.61±0.11	1.25±0.02
F4	24.51±0.16	0.35±0.01	0.45±0.01	15.33±0.15	1.24±0.01
F5	22.60.21	0.35±0.01	0.44±0.00	15.25±0.05	1.25±0.02

Table. No: 6 Table showing pre-compression values of the F6-F9

Post compression parameters for F1-F5 Formulations:

Formulation	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F6	24.38±0.13	0.32±0.02	0.41±0.02	14.28±0.13	1.24±0.01
F7	24.52±0.28	0.31±0.02	0.40±0.04	13.18±0.04 1.	1.21±0.01
F8	23.39±0.19	0.34±0.00	0.42±0.01	14.31±0.11	1.24±0.02
F9	23.61±0.16	0.34±0.01	0.42±0.01	14.23±0.15	1.23±0.01

Table. No: 7 Table showing post compression values from F1-F5

Pre compression parameters for F6-F9 formulations:

Formulation	Weight variation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)	Disintigration (min)
F1	198±1.02	2.50±0.01	3.5±0.06	0.632	97.24±0.22	25
F2	198±0.08	2.65±0.00	3.6±0.06	0.646	96.57±0.42	24

F3	199.002	2.7±0.01	3.5±0.00	0.686	97.43±0.13	24
F4	198±0.003	2.58±0.01	3.85±0.06	0.526	97.83±0.42	24
F5	199±0.08	2.42±0.01	3.7 ±0.10	0.546	97.86±0.32	24

Table. No: 8 Table showing post compression values of the F6-F9

All the post compression parameters are come under the within range of limits

***In –vitro* drug release studies for all formulations:**

Formulation	Weight variation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)	Disintigration (min)
F6	**200** ±1.02	**2.50**±0.01	**3.5**±0.06	**0.622**	**98.24**±0.22	**25**
F7	**200**±0.08	**2.65**±0.00	**3.6**±0.06	**0.600**	**99.57**±0.42	**24**
F8	**200.002**	**2.7**±0.01	**3.5**±0.00	**0.636**	**98.43**±0.13	**25**
F9	**199**±0.003	**2.58**±0.01	**3.85**±0.06	**0.656**	**98.83**±0.42	**26**

DISCUSSION

Table. No: 9 Table showing *In-vitro* drug release studies of the all formulations

Time in hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	20.32	15.52	17.32	17.15	18.32	22.52	22.65	23.15	24.21
2	17.62	21.52	23.52	24.15	27.53	31.53	38.62	31.15	35.65
3	23.31	25.12	25.13	32.45	38.65	49.72	44.56	41.12	41.52
4	25.61	35.46	36.25	41.13	44.55	51.62	57.62	55.32	55.22
5	36.21	42.15	47.12	51.18	57.18	69.43	68.65	63.63	62.23
6	52.53	51.32	54.12	62.25	69.83	76.53	73.65	74.65	70.23
7	72.65	59.65	64.56	72.45	76.13	79.65	87.65	85.65	80.23
8	85.32	65.32	75.32	78.25	82.12	86.35	92.23	92.56	90.56
9	90.32	75.16	80.41	83.13	93.12	94.56	99.55	97.65	96.86

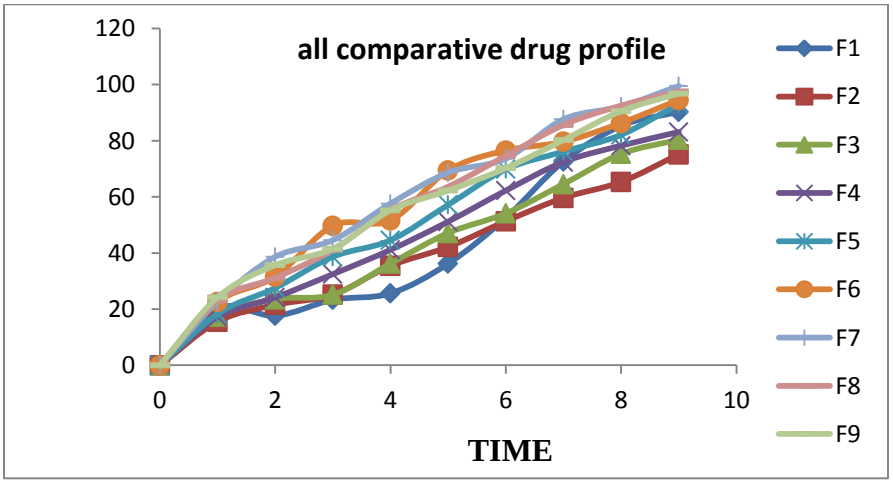


Fig. No: 3 Picture showing all comparative studies of the F1-F9

Comparative profile for F1-F3

Table. No; 11 Table showing comparative studies of the F1-F3

Time in hrs	F1	F2	F3
0	0	0	0
1	20.32	15.52	17.32
2	17.62	21.52	23.52
3	23.31	25.12	25.13
4	25.61	35.46	36.25
5	36.21	42.15	47.12
6	52.53	51.32	54.12
7	72.65	59.65	64.56
8	85.32	65.32	75.32
9	90.32	75.16	80.41

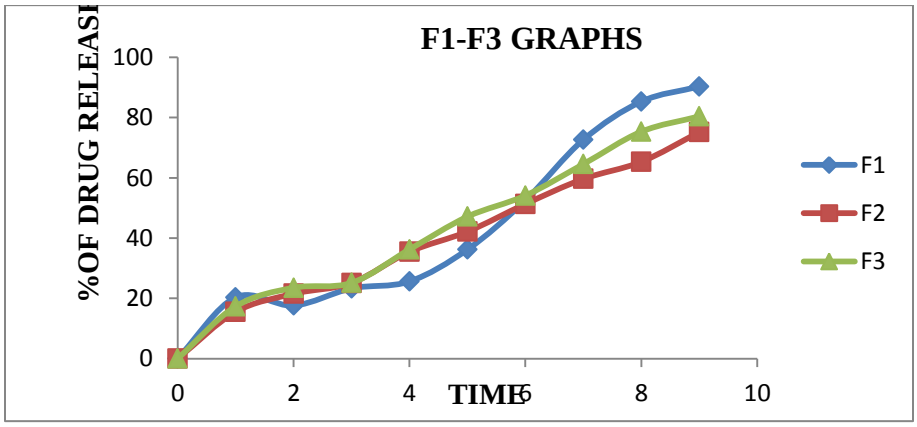


Fig. No: 4 Picture showing comparative graph of F1-F3

Comparative profile for F4-F6

Table. No: 12 Table showing comparative drug release studies values from F4-F6

Time in hrs	F4	F5	F6
0	0	0	0
1	17.15	18.32	22.52
2	24.15	27.53	31.53
3	32.45	38.65	49.72
4	41.13	44.55	51.62
5	51.18	57.18	69.43
6	62.25	69.83	76.53
7	72.45	76.13	79.65
8	78.25	82.12	86.35
9	83.13	93.12	94.56

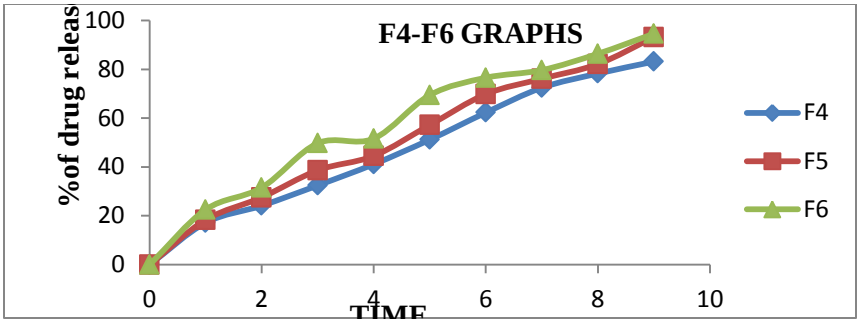


Fig. No: 5 Picture showing comparative graph of F4-F6

Comparative profile for F7-F9

Table.No:13 Table showing comparative drug release studies values from F7-F9

Time in hrs	F7	F8	F9
0	0	0	0
1	22.65	23.15	24.21
2	38.62	31.15	35.65
3	44.56	41.12	41.52
4	57.62	55.32	55.22
5	68.65	63.63	62.23
6	73.65	74.65	70.23
7	87.65	85.65	80.23
8	92.23	92.56	90.56
9	99.55	97.65	96.86

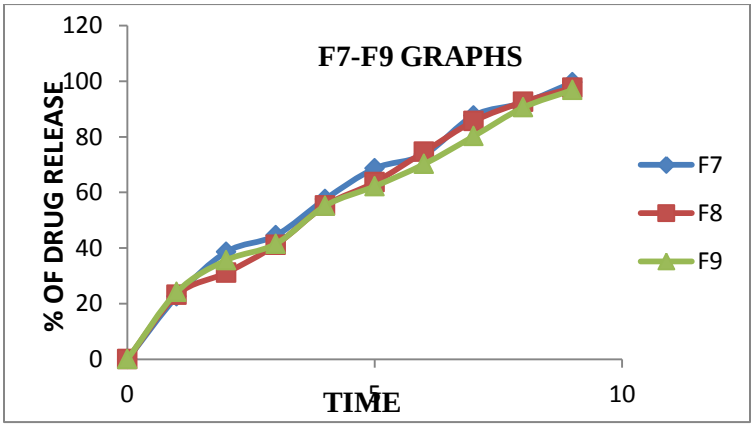


Fig. No: 6 Picture showing comparative graph of F7-F9

Kinetic studies for optimized formulation (F7)

Table. No: 14 Table showing kinetic profile data

Time	%cdr	Log T	√T	Log%cdr	ARA	Log%ARA
0	0	1	0	1	100	2
1	22.65	0	1	1.373	77.35	1.882
2	38.62	0.303	1.414	1.597	61.38	1.7808
3	44.56	0.472	1.732	1.658	55.44	1.7359
4	57.62	0.66	2	1.775	42.38	1.6061
5	68.65	0.697	2.236	1.842	31.35	1.4821
6	73.65	0.771	2.449	1.873	26.35	1.4039

7	87.65	0.848	2.645	1.947	12.35	1.0549
8	92.23	0.909	2.828	1.978	7.77	0.678
9	99.55	0.9543	3	1.998	0.45	0.346

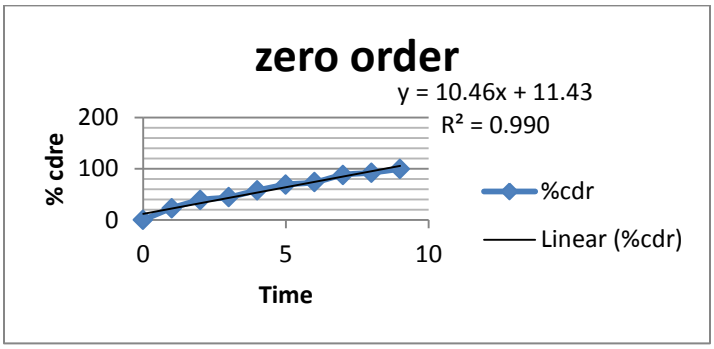


Fig. No: 7 Picture showing zero order kinetic graph of F7

First order

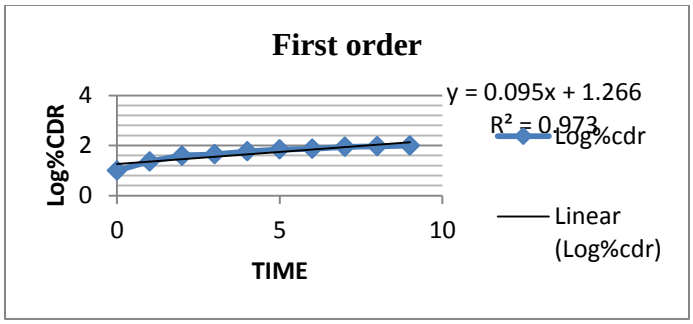
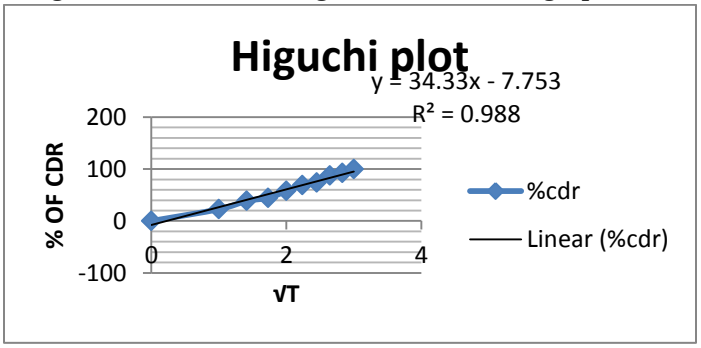


Fig. No: 8 Picture showing first order kinetic graph of F7



Higuchi order: Fig no: 9 Picture showing higuchi kinetic graph of F7

Korsmeyer Peppas plot

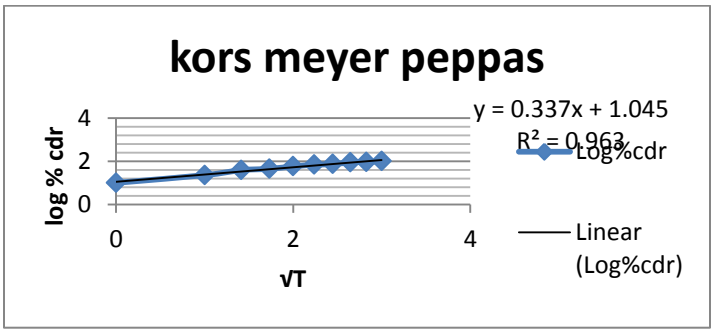


Fig. No: 10 Picture showing korsmeter kinetic graph of F7

Table. No: 15 Table showing values of the kinetic data

S.no	Zero order	First order	Higuchi	Krossmayer peppas
Code	R^2	R^2	R^2	R^2
F9	0.990	0.973	0.988	0.963

STABILITY RESULTS

Stability samples are stored at

- Accelerated: 40±2^{0}C/75±5% RH
- Intermediate: 30±2^{0}C/65±5% RH
- Long term: 25±2^{0}C/60±5% RH

Testing Intervals

- Accelerated: Initial, 3months.

Table no: Results of stability studies of optimized formulation F-7

Formulation Code	Parameters	Initial	1st month	2nd month	3rd Month	Limits as per Specifications
F-7	25^{0}C/60%RH	99.55		99.76	99.63	Not less than
	% Release		99.59			85 %
F-7	30^{0}C/75% RH	99.55		99.82	99.84	Not less than
	% Release		99.68			85 %
F-7	40^{0}C/75% RH	99.55		99.65	99.76	Not less than
	% Release		99.75			85 %

CONCLUSION

The gastro retentive tramadol hcl tablets prepared by using different excipients .The before going to formulate the tablets the preformulation studies are carried out such as FTIR, calibration, organoleptic characters. The formulation is developed by using polymers such as HPMC K4M and xanthin gum used in different trails. The pre compression parameters such as angle of repose, bulk density, true density, compressibility index, these are found to be within the limits. The tablets of tramadol hcl gastro retentive tablets are prepared by direct compression method. The talc used as glident and lactose used as lubricant mcc used as filler. The after development of gastro retentive tablets of tramadol hcl they undergo for evaluation parameters. Such as weight variation, thickness, friability, drug content, disintegration, and In vitro dissolution studies. They all are found in within range of limits. The in vitro drug release studies carried out by USP-II apparatus. The buffer medium 6.8 .The optimised formulation F7 undergo for mathematical modelling to know about the diffusion mechanism .it fallows the zero order higuchi equation. The optimised formulation undergo for stability studies for 90days.In stability studies the drug content and drug release studies carried out. These no degradation takes place in the drug content and drug release studies.

REFERENCES

[1]. S. Li et. al., Statistical optimization of gastric floating system for oral controlled delivery of calcium. AAPSPharmSciTech 2(1), 2001, article1.

[2]. R. Talukder and R. Fassihi, Gastroretentive Delivery Systems: A mini Review. Drug Development and Industrial Pharmacy 30(10), 2004, 1019-1028.

[3]. R. Hejazi and N. Amiji, Stomach specific anti H.Pylori therapy. I: Preparation and characterization of tetracycline of a floating multiple unit capsule, a high density loaded chitosan microspheres. Int. J. Pharm. 235, 2002, 87-94.

[4]. M P Cooerman, P Krausgrill, K J Hengels, Local gastric and serum amoxicillin concentration after different oral application forms. Antimicrob Agents Chemother 37, 1993, 1506150g.

[5]. B S Dave, A F Amin, M Patel, Gastroretentive drug delivery system of Ranitidine HCl formulation and in vitro evaluation. AAPS PharmSciTech; 5, 2004, 1- 10.

[6]. W Sawicki, Pharmacokinetics of verapamil and nor verapamil from controlled release floating pellets in humans. Eur J Pharm Biopharm; 53, 2002, 29-35.
[7]. B M Singh and K H Kim, Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. J Control Release 63, 2000, 235-259.
[8]. S K Jain, G P Agarwal, N K Jain, Evaluation of porous carrier based floating orlistat microspheres for gastric delivery. AAPS PharmSciTech; 7(4), 2006, 90.
[9]. P Sriamornsak, N Thirawong, S Puttipipatkhachorn, Morphology and buoyancy of oil entrapped calcium pectinate gel beads. The AAPS Journal; 6(3), 2004, Article 24.
[10]. J M Patil, R S hirlekar, P S Gide and V J Kadam, Trends in floating drug delivery systems. J SCI IND RES; 65, 2006.