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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF POORLY WATER SOLUBLE DRUG LOPERAMIDE HCL

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ABSTRACT

The fast-dissolving tablet (FDT) is an innovative and unique drug delivery system that is rapidly gaining attention in fast-dissolving technology research. Fast dissolving tablets are proving to be one of the most popular and widely accepted dosage forms, especially in pediatric patients due to incomplete development of muscles and nervous system and in geriatric patients suffering from Parkinson's disease or hand tremors. The oral dosage form and route is the most preferred route of administration for various drugs that have limitations such as e.g. First-pass metabolism, psychiatric patients, disabled and uncooperative patients. FDTs break down or quickly dissolve in saliva without the need for water. The FDTs formulation contains Superdisintegrants to increase the rate of dissolution of a tablet in the oral cavity. FDT have advantages such as easy portability and formulation, accurate dosage, good chemical and physical stability, and is an ideal choice for geriatric and pediatric patients. FDTs are rapidly degraded, rapidly absorbed and therefore improve the release time of the drug in vitro and this property of the drug (dosage form) increases bioavailability. This review article covers different FDT techniques, criteria of FDT, advantages and disadvantages of FDT, selection of superdisintegrants, different patented technologies, challenges faced FDT, evaluation parameters of FDT, marketed preparation of FDT.

Keywords : Fast Dissolving Tablet, Oral drug delivery system, solid dispersion, super disintegrants.

Introduction: An oral route remains most popular route of administration of therapeutic agents. For better patients compliance it should not disturbed his daily routine life style and it should be expectable aesthetically, organoleptically, therapeutically and for economic point. The oral dosage forms are present in different strength; provide flexibility of dose to suit different age group or for different disease condition. The oral dosage forms must retained the shape, size, appearance, taste, flavor and therapeutic effect during stipulated shelf life.

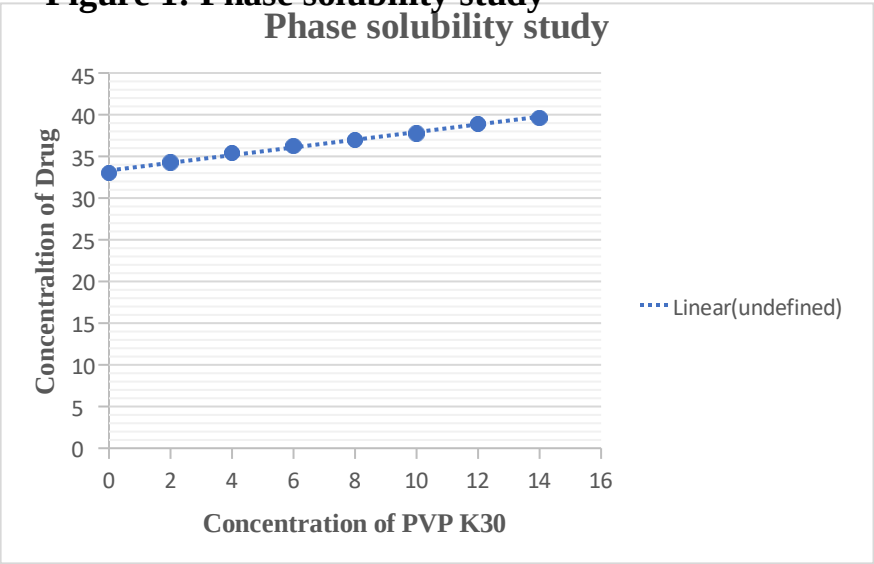
Materials and Method : Loperamide was procured from Schwann pharma Indore (M.P.) India. and PVP K-30 were of pharmaceutical greade and obtained from Loba Chemie Pvt. Ltd. Mumbai. . Crospovidone, Sodium starch glycolate , Croscarmellose sodium procured from Lupin Research Center pune (M.H.) India. Microcrystalline cellulose, Mannitol procured from Plethico pharmaceuticals Ltd. Indore (M.P.). Talc, Magnesium Stearate was purchased from Loba Chemie Pvt. Ltd. Mumbai. All solvent used were of analytical greade and were purchased from Merck Ltd. Mumbai (M.H.) India.

FORMULATION AND OPTIMIZATION OF FDTs

phase solubility Study

Excess amount of Loperamide HCL was added to 10 ml of aqueous solution containing various concentration of PVP K30 (1%-14%) take in a series of capped vials and mixture were shaken for 48 hours at room temperature on a rotary shaker. The supernatant solutions were collected care fully and filtered by using what's man filter paper. The filtered sample were diluted suitably and assayed for Loperamide HCL by measuring absorbance at 420 nm against blank prepared in same concentration of PVP K30 in water. A phase solubility diagram is constructed by plotting the molar Concentration of dissolved Loperamide HCL, found on vertical axis, against the Concentration of PVP K30 added on the horizontal axis (Figure 1) (Swarbick, 2007) .

Figure 1: Phase solubility study



The solubility of Loperamide HCL increase with increase in concentration of PVP K30 and hence, phase solubility diagram could be A_L type. The host-guest correlation coefficient R^2

0.992 and slope of 0.460 indicated that a complex of 1:1 molar ration was formed.(Swarbrick et al., 2007)

Preparation of solid dispersion of Loperamide HCL with PVP K30 Loperamide HCL and PVP K30 was dissolved in a common solvent. The mixture was stirred for 15 min solvent evaporated and dried until dryness. The dried mass pulverized and sieved no. 44. After drying, solid dispersion of Loperamide HCL and PVP K30 was obtained. (Islam et al., (2012)

Quantitative estimation

Calibration Curve of Loperamide Hydrochloride

Preparation of Stock Solution

100 mg of Loperamide Hydrochloride was accurately weighed and transferred to 100 ml volumetric flask. The drug was dissolved in 0.1N HCL to get a solution of 1000µg/ml (stock solution I) . 10 ml of the above solution was taken and diluted to 100 ml with 0.1N HCL (stock solution II) . Then 10 ml of the above stock solution II was diluted up to 50 ml with methyl orange solution (1% w/v) and extracted with chloroform (3x15 ml). Organic layers were separated and pooled. The volume of pooled organic layer was made up to 100 ml with sodium acetate solution (stock solution III). This stock solution III was used to prepare a series of standard Loperamide solutions as discussed below .

PROCEDURE

From stock solution III samples of 1,2,3,4,5,6,7& 8 ml were transferred to a series of 10 ml Volumetric flask 0.1N HCL was used to make up the volume to obtain 10,20,30,40,50,60,70 &80 µg/ml of Loperamide HCL. The absorbance of these solutions was measured at 420 nm against blank. The data are recorded and the curves are plotted.

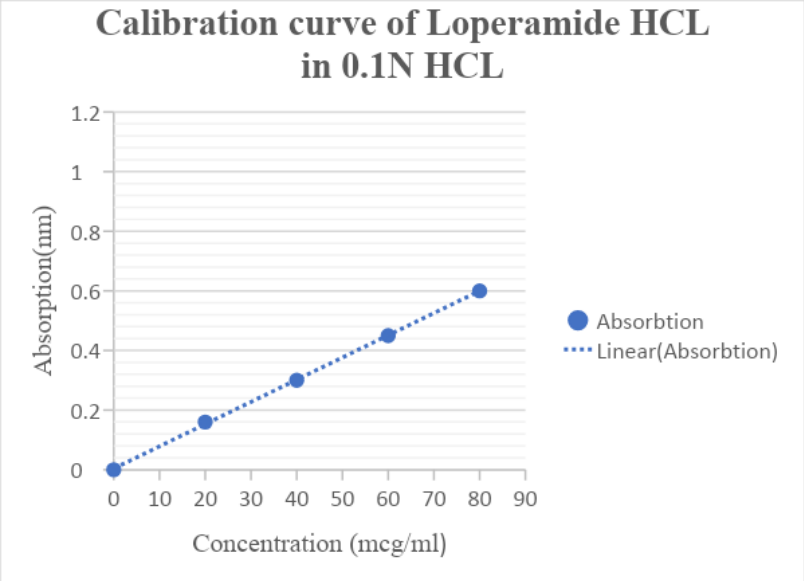


Figure 2: Calibration curve of Loperamide HCL in 0.1N HCL

Formulation of Fast Dissolving tablet of Loperamide

Drug polymer complex (solid dispersion) and all excipients were passed through sieve no 60. Drug polymer complex, directly compressible Mannitol, Superdisintegrants (Sodium starch glycolate, Croscarmellose Sodium or Crospovidone), Microcrystalline Cellulose, Talc were mixed together for 20 min. Magnesium stearate, was then added and mixed for 5 min. Then blend of drug and Excipients to compress on Single punch machine Table 2.

Table 1: Formulation of Fast Dissolving Tablets

Ingredients	**Quantity (mg)**								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Solid dispersion (equiblent 8mg drug)	40	40	40	40	40	40	40	40	40
SSG	2 (1%)	6 (3%)	10 (5%)						
CC				2(1%)	6(3%)	10(5%)			
CP							2(1%)	6(3%)	10(5%)
Mannitol	143	139	135	145	139	135	143	139	135
Mcc	30	30	30	30	30	30	30	30	30
Talc	2	2	2	2	2	2	2	2	2
Mg stearate	2	2	2	2	2	2	2	2	2
total	220	220	220	220	220	220	220	220	220

FTIR STUDIES FTIR Spectroscopy studies a sample drug of Loperamide HCL the active pharmaceutical ingredients.

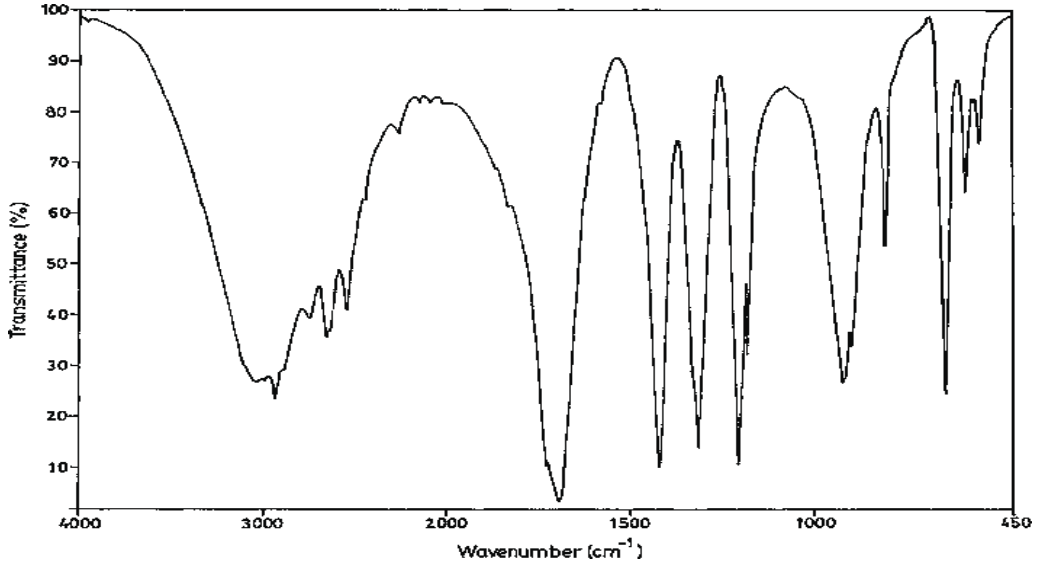


Figure 3: FTIR Spectrum Of Sample Drug Loperamide HCL

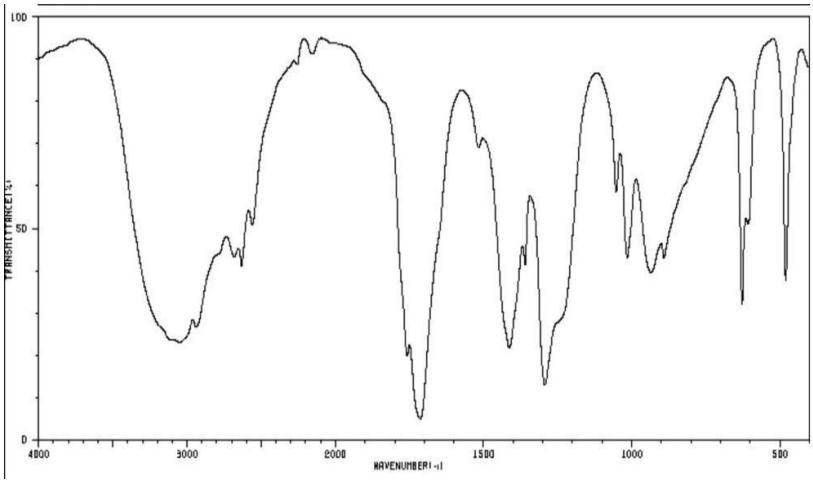


Figure 4:FTIR Spectrum Of Loperamide HCL and PVP K30 Solid dispersion

Evaluation of Fast Dissolving Tablets

Table 2 Evaluation of Fast Dissolving Tablets

Parameters	**Formulation batch no.**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Hardness Kg/*cm*²	2.6	2.7	2.8	2.7	2.7	2.6	2.7	2.7	2.8
Friability (%)	0.42	0.57	0.52	0.51	0.52	0.41	0.43	0.47	0.43
Weight variation test	120.046± 1.3	121.52 ± 1.2	123.56 ± 1.1	120.11 ± 1.4	122.11 ± 1.9	120.74 ± 1.6	124.56 ± 1.2	124.64 ± 1.6	123.74± 1.3
Wetting Time (sec)	26	22	19	22	21	19	22	21	20
Disintegration Time (sec)	30	29	27	31	32	28	28±1.3	32±2.2	27 ± 1.5
Dispersion Time (sec)	60.72	46.82	49.42	58.92	51.89	52.30	54.24	57.27	57.28
Drug content (%)	97.87	95.52	98.40	99.12	95.59	96.95	99.20	97.32	98.45

In vitro drug release

İn vitro dissolution study of drug was performed in 900 ml phosphate buffer pH6.2 using USP type II (paddle apparatus at 50 rpm for 15 min (37±0.5°C). A dissolution medium (5ml) as a sample with drawn at specific time interval (2, 4, 6,8, 10, and 15) replaced equal volume of fresh medium immediately. The samples were filtered from 0.22 micrometer membrane filter disc and filtrate was measure for drug content at 420 nm. Drug concentration was recorded by the calibration curve and expressed as cumulative percent drug release. (Table:3) (Amman age et al.,2011; Keshav et al.,2012).

Table 3 : Dissolution profiles of FDTs

Time (min).	**Cumulative % drug release of different Formulations**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
2	14.25± 1.6	17.81 ± 2.4	18.91 ± 1.6	41.74 ± 0.8	49.47 ± 1.3	52.30 ± 4.2	60.15 ± 2.5	52.28 ± 3.4	42.24 ± 1.2
4	25.79 ± 1.2	38.27 ± 1.6	37.29 ± 1.7	63.46 ± 2.9	53.64 ± 3.2	63.12 ± 1.2	76.91 ± 3.4	65.54 ± 2.7	55.42 ± 1.03
6	37.71 ± 1.0	48.72 ± 2.1	51.82 ± 1.9	72.49 ± 1.87	68.84 ± 1.7	72.54 ± 0.6	87.44 ± 1.5	79.34 ± 0.8	75.91 ± 2.3
8	49.81 ± 1.5	60.62 ± 2.4	62.92 ± 1.3	80.41 ± 2.6	79.43 ± 2.6	83.68 ± 2.6	90.25 ± 2.2	82.25 ± 0.4	80.04 ± 2.26
10	67.81 ± 1.2	69.29 ± 1.5	77.32 ± 1.9	90.04 ± 2.5	88.94 ± 4.5	90.25 ± 1.5	94.34 ± 3.9	86.94 ± 3.9	89.65 ± 0.8
12	82.27 ± 1.8	87.92 ± 1.7	89.22 ± 1.2	96.64 ± 1.5	92.94 ± 5.1	94.65 ± 1.1	97.10 ± 1.3	88.25 ± 1.6	95.70 ± 1.2
15	94.38 ± 1.7	93.84 ± 1.6	96.92 ± 1.6	97.89 ± 1.3	93.69 ± 1.7	94.60 ± 1.0	98.12 ± 1.1	95.48 ± 1.7	97.53 ± 1.9

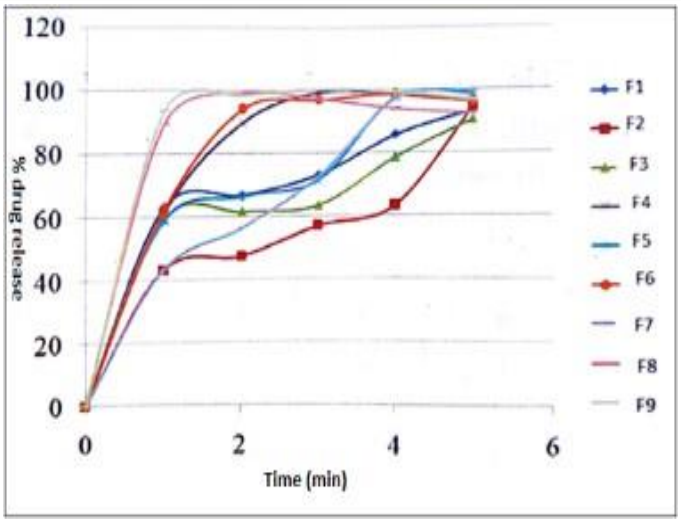


Figure 5: % cumulative drug release of F1 -F9

Result and discussion After pre-compressed test the powder blends of all the formulation was compressed into tablet and it was evaluated on the basis of various factors which include hardness, friabi1ity, weight variation, dispersion time, wetting time, disintegration time, drug content, In-Vitro drug release.

Fast disintegrate tablet was formulated with different concentration of Sodium starch glycolate (SSG) in (1%, 3%, 5%) and 5% concentration of SSG gives best value of wetting time 19 ± 2.24 sec, disintegration time 27 ± 1.6 sec, dispersion time 49.42 sec, and dissolution profile with maximum % cumulative drug release 96.92 ± 1.6 % in 15 min.

Fast disintegrate tablet was formulated with different concentration of Croscarmellose (CC) in (1%, 3%, 5%) and 1% concentration of CC gives best value of wetting time 22 ± 2.60 sec, disintegration time 31 ± 3.0 sec dispersion time 58.92 sec, , and dissolution profile with maximum % cumulative drug release 97.89 ± 1.3 % in 15 min.

Fast disintegrate tablet was formulated with different concentration of crosspovidone (CP) in (1%, 3%, 5%) and 1 % concentration of CP gives best value of wetting time 22 ± 2.2 sec, disintegration time 28 ± 1.3 sec, dispersion time 54.24 sec, and dissolution profile with maximum % cumulative drug release 98.12 ± 1.1 % in 15 min

Thus, according to all evaluation parameters, Cross povidone at 1% concentration was found to be the best superdisintegrant among SSG, CCS, and CP for formulation of Fast dissolving tablet of Loperamide HCL and FDT incorporating CP at 1% concentration emerged as the optimized formulation.

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