Formulation and evaluation of orodispersible liquisolid tablets of Haloperidol

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***Abstract*: The present study aimed to enhance the dissolution rate of a poorly water-soluble drug, Haloperidol by adopting liquisolid compact technique and formulating it into an orodispersible system to overcome the gastric metabolism of the drug. Here 12 different formulations of liquisolid compacts of Haloperidol were formulated by varying the concentration of drug solution from 10-30%w/v. Avicel pH 102 and Aerosil 200 was used as carrier and coating material respectively. Crospovidone and SSG in the ratio of 1:1 were added to the formulation for faster disintegration. Prior to the compression of orodispersible tablets all the 12 batches of liquisolid compacts were subjected to precompression evaluations and the results were found to be satisfactory. Further, the prepared powder blends were directly compressed into orodispersible liquisolid tablets. The orodispersible liquisolid tablets were evaluated for the post-compression parameters like weight variation, hardness, friability, disintegration test, wetting time, water absorption ratio, drug content, and in-vitro dissolution studies. From the obtained results, it could be concluded that the formulation LS2 with 10% concentration of drug solution and carrier to coating material in the ratio of 20:1, exhibits quick disintegration and had a maximum drug release of 98.1% at the end of 30 minutes. Liquisolid tablet (LS2) demonstrated a significantly higher drug release rate than those of marketed tablet, which may be due to enhanced wetting properties and increased effective surface area of the drug. The results of the kinetic study revealed that the formulation followed first-order kinetics with a dissolution-controlled release pattern. From the results of stability studies, the batch was found to be stable. In conclusion, the liquisolid compacts technique can be a promising alternative for the formulation of water-insoluble drugs, such as Haloperidol into rapid-release tablets. In conclusion, combining the liquisolid technology and orodispersible system can be used as a promising alternative to improve the dissolution rate of poorly water soluble drugs like Haloperidol.**

***Keywords*: Liquisolid technique, Haloperidol, orodispersible tablets.**

I. INTRODUCTION

Most of the newly developed active pharmaceutical ingredients are having low water solubility, which is a substantial problem confronting the pharmaceutical industry for designing of new dosage forms[1]. Because solubility is one of the critical parameter for achieving desired concentration of the drug in systemic circulation to achieve a required therapeutic response. Poor water soluble drugs require more time to dissolve in the gastrointestinal fluid under normal conditions that may delay the absorption of the drug to the systemic circulation. Hence to improve the water solubility and bioavailability of these kind of drugs we can adopt curtain major formulation tools like solid dispersion, cyclodextrin complexation, micronization and liquisolid tecnique etc[1,2]. Out of these liquisolid compact technique is a new and promising addition towards such a novel aim[3].

The liquisolid technology is first outlined by spireas et al in 1998. It is refers to the formulations which are prepared by converting a liquid drug or a drug in liquid state (solutions, suspensions, or emulsions) into dry, non-adherent, free-flowing, and readily compressible powder mixtures. It is achieved by blending or spraying a liquid dispersion onto specific powder carriers and coating materials[4]. Here the drug will be held within the powder substrate in solution, or a solubilized molecularly dispersed state. So it improves the wetting property and surface area available for dissolution, which results in an enhanced drug release rate and consequently improved bioavailability. And also as compared to all other mentioned techniques, liquisolid compact system is simple, easy to scale up, and has low cost formulation strategy for improving the dissolution rate of the poorly soluble drugs[5].

Commercially fast disintegrating tablets are widely accepted in order to improve the ease of drug administration. In addition to ease of drug administration, fast disintegrating tablets have been investigated for their potential in increasing the bioavailability of poorly water-soluble drug, by enhancing the dissolution profile of the drug. This also provide rapid onset of action, by avoiding the need for gastric disintegration and facilitating pre-gastric absorption. Fast dissolving tablets also provide easy manufacturing accurate dosing and good stability[6].

Haloperidol is an Antipsychotic drug belongs to class II drug as per BCS classification and the bioavailability was found to be only 70% when administered orally[7]. This lesser bioavailability may be due to the poor solubility and also high gastric metabolism rate of drug. Hence, the present study deals with the dissolution enhancement of Haloperidol by adopting liquisolid technique and an attempt would be planned to formulate it into orodispersible tablets in order to overcome these problems related to the drug. In psychiatric patients ODTs are providing greater advantages compared to conventional dosage forms. So formulating orodispersible liquisolid tablets is a successful and promising dosage form for the delivery of Haloperidol[8].

II. MATERIAL AND METHODS

MATERIALS

The materials used for the formulation of dosage form were; Haloperidol, Sodium starch glycolate, Aerosil 200 (Yarrow chemicals, Mumbai); Avicel PH 102, Crospovidone, Aspartame and Mannitol (Balaji chemicals, Gujarat) Magnesium stearate (Loba chemicals, Mumbai) Propylene glycol (PG) (Medilise chemicals, Kannur).

METHODS

Analytical methods

Haloperidol was dissolved in phosphate buffer pH 6.8 to produce a 10µg/ml solution. Λ_{max} of this solution was measured by using UV spectrophotometer in the range of 200-400nm[7].

Standard curve of Haloperidol

A stock solution of Haloperidol 500µg/ml was prepared using phosphate buffer pH 6.8. This solution was further diluted to obtain 5, 10, 15 and 20µg/ml solution and the absorbance was measured by using UV visible spectroscopy at 248nm[7].

Saturation solubility

Solubility studies of Haloperidol were carried out in solvents such as distilled water, methanol, propylene glycol and poly ethylene glycol. Here to determine solubility super saturation method was employed. 5ml of solvent was taken, and the drug was gradually added to get a supersaturated solution. The test tube was then shaken for 24 hours and filtered. Then solubility of the sample was then determined by using uv-visible spectrophotometer at 248 nm[8,9]. Results were reported in Table 3.

Determination of melting point

The open capillary method was used to determine the melting point of pure Haloperidol with the help of Thiel's apparatus.

Drug excipient interaction study

To study the compatibility of the drug with excipients such as carrier, coating material and superdisintegrants act. The compatibility study was done by FTIR spectroscopy using the KBr pellet technique[10].

FORMULATION DESIGN OF ORODISPERSIBLE LIQUISOLID TABLETS OF HALOPERIDOL.

Formulation of orodispersible liquisolid tablets of Haloperidol includes two technique i.e., formulation of liquisolid compact of Haloperidol and conversion of prepared compacts into orodispersible tablets.

Since the solubility of Haloperidol was very less in water we have dissolved the Haloperidol in a non-volatile solvent and then converted to solid dosage form with the help of a carrier and coating material added to it. The drug will be retained as a liquid in the soluble state within the product but outer part will be serves as a solid due to the presence of carrier and coating material.

Preparation of liquisolid compacts

Here PG was selected as a non-volatile solvent. MCC and Aerosil 200 were used as carrier and coating material respectively. Now the amount of carrier and coating material for the specific batches were determined by using spireas equation.

Determination of loading factor

By substituting the liquid retention potential value of the carrier (C_A-value) and the coating material (C_O-value) into Equation 1, the loading factor can be computed.

$$Lf = \Phi_{CA} + \Phi_{CO}\,(1/R) \longrightarrow 1$$

Where, Ø value of the powder is the maximum amount of a given non-volatile liquid that can be retained inside the powder bulk (w/w) while maintaining acceptable flowability. It was calculated by (Equation 2) the following procedure, 5g of each powder (carrier and coating material) was taken and increasing amount of liquid vehicle was added. Ø value and angle of repose was calculated for powders after each time addition of vehicle. Then, a graph is plotted with angle of repose on Y-axis and Ø value on X- axis. The liquid retention potential value of the excipient can be determined by choosing the Ø value that corresponds to angle of repose of 33°[11,12].

$$Ø = \frac{weight\ of\ liquid}{weight\ of\ solid} \longrightarrow 2$$

The loading factor has to be determined for each carrier to coating material ratio (R) (given in Table 1) with the help of Ø value obtained. The amount of carrier and coating material for the formulation of liquisolid compacts were estimated by substituting these values in Equation 3 and 4[13].

$$R = Q/q \longrightarrow 3$$

$$Lf = W/Q \longrightarrow 4$$

For the preparation of liquisolid compacts the drug is dissolved in non-volatile solvent (PG) and this drug solution was added to the calculated amount of carrier material and triturated well. The preparation was kept aside for one min in order to complete absorption of liquefied drug in to the porous carrier material. Then weighed amount of coating material was added and triturated slowly for 5 another minutes for the complete absorption of coating material over the porous carrier material so as to convert the mixture to free flowing powder. To these 12 batches of liquisolid compacts prepared with varying ratios of carrier and coating material superdisintegrants crospovidone and SSG should be added to obtain a faster disintegration once they are compressed. The Lf values for different ratios of carrier and coating material are given in Table 5.

Optimization of concentration of superdisintegrants

The formula of formulation LS1 was chosen to study the effect of various superdisntegrants and their concentration which was a requisite for ODT tablets. Four different batches FS1-FS4 were formulated with varying concentration of superdisintegrants in the ratio of 1:1. The concentration of superdisintegrants ranged from 5-12.5mg. The dissolution and disintegration profiles of the

prepared formulations were observed, and the superdisintegrats concentration at which the maximum percentage of drug release achieved was chosen.**Pre compression evaluations**

To 12 batches of liquisolid compacts prepared, the other excipients for the tablet formulations were added. Which included crospovidone & SSG-7.5mg (superdisintegrants), Aspartame-5% (sweetening agent), Mannitol (diluent), and Magnesium stearate-1% (glidant). These prepared powder blends were subjected to precompression evaluations such as angle of repose, bulk density, tapped density, compressibility index, and Hausners' ratio to determine the flow property of the prepared powder blend[14,15]. Results were repored in Table 6.

Preparation of orodispersible liquisolid tablets of Haloperidol

The formulas of 12 different batches of liquisolid ODTs were given in Table 2. Batches LS1-LS4, LS5-LS8 and LS9-LS12 were prepared using 10, 20 and 30% concentration of drug solutions respectively. The formulated 12 batches of liquisolid compact powder blend containing 2mg of Haloperidol were directly compressed into tablets by using rotary tablet punching machine.

Table 2: Formulation design of Haloperidol liquisolid tablets containing 10% drug solution 20% of drug solution & 30% of drug solution.

Ingredients (mg)	**LS1**	**LS2**	**LS3**	**LS4**	**LS5**	**LS6**	**LS7**	**LS8**	**LS9**	**LS10**	**LS11**	**LS12**
Haloperidol	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
PG	**20.0**	**20.0**	**20.0**	**20.0**	**10.0**	**10.0**	**10.0**	**10.0**	**6.6**	**6.6**	**6.6**	**6.6**
MCC 102	153.8	173	181.8	185.1	76.92	86.9	90.9	92.5	47.1	55	58.40	59.45
Aerosol 200	15.3	8.65	6.06	5.2	7.6	4.3	3.0	2.6	4.71	2.75	1.94	1.69
SSG	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Crospovidone	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Mg stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Aspartame	5	5	5	5	5	5	5	5	5	5	5	5
Mannitol	36.3	23.8	17.6	15.2	130.98	124.3	121.6	120.4	167.0	161.1	158.56	157.7
Unit weight	250	250	250	250	250	250	250	250	250	250	250	250

Post compression evaluations

Thickness and Hardness

The thickness and hardness of the tablets were measured by using vernier calliper and Monsanto hardness tester respectively[16] and the results were reported in Table 7.

Friability test

Roche friabilator was used to assess the tablets' friability. The percentage friability of the tablets can be calculated by the eq below [9,16] and reported in Table 7.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

Weight variation test

The test was performed as per USP by weighing 20 tablets individually on electronic balance. Weight of the individual tablets were compared to weight of 20 tablets and reported in Table 7.

Wetting time

A folded piece of tissue paper which was sufficiently wetted was placed in a tiny petridish. Then the tablet was placed on the paper, and the time taken for the tablet to wet completely was noted [9,16]and reported in Table 7.

Water absorption ratio

The weight of the tablet before (Wb) and after (Wa) wetting were noted. The water absorption ratio (R) was then calculated using the Equation below[17] and results were reported in Table 7.

$$R = 100 \times \frac{(Wa - Wb)}{Wb}$$

In-vitro disintegration time

The modified disintegration method was used to determine the disintegration time of the prepared tablets. A petridish (10 cm diameter) was filled with 10 ml phosphate buffer for this purpose. The tablet was carefully placed in the middle of petridish, and the time taken for the tablet break down into fine particles was noted[18,19].

Drug content determination

Five randomly selected tablets were weighed and powdered in a glass mortar. The powder sample equivalent to 2mg was then precisely weighed and dissolved in a small amount of methanol before being diluted with phosphate buffer pH 6.8 to reach a volume of 100ml; the absorbance was measured spectrophotometrically at 248 nm[9,17].

In- vitro drug release study

In- vitro dissolution studies were carried out using USP apparatus type II at 50 rpm. Dissolution medium consisted of 500 ml phosphate buffer pH 6.8 maintained at $37^0C \pm 0.5^0C$. Drug sample (5ml) was withdrawn at 1, 2, 3, 5, 10, 20 and 30 min time intervals and absorbance was measured in uv-visible spectrophotometer at 248 nm. The samples were replaced with fresh dissolution medium[9,20].

Comparison of optimized formulation of Haloperidol with DCT and conventional marketed formulation.
To study the percentage increase in drug release the selected formulation LS2 was compared with standard Haloperidol commercial formulation. Further, DCTs of Haloperidol were formulated in the lab and compared with the obtained results of optimized formulation of orodispersible liquisolid tablet to confirm that the increased drug release was not only due to the effect of superdisintegrants but also due to the adopted liquisolid technique used for the formulation of ODTs.

Scanning electron microscope
SEM analysis study was conducted for the selected LS2 formulation and the results obtained were compared with the SEM analysis of the pure drug to study the change in surface properties of the pure drug[15].

Drug release kinetics
To determine the release mechanism from formulation, the regression coefficients of various kinetic models were performed, including zero-order, first order, higuchi and Hixson-Crowell.

Stability studies[16]
Stability studies were carried out for the optimized formulation LS2 according to international conference of Harmonization (ICH) guidelines.
The optimized formulations were stored at 40±2^{0}C/ 75±5% RH for 45 days. After the stability period, samples were taken and analyzed for the friability, hardness, disintegration, % drug content and in-vitro drug release study[16].

III. RESULTS AND DISCUSSION

UV analysis
The λ_{max} Haloperidol was found to be 248nm (Figure 1).

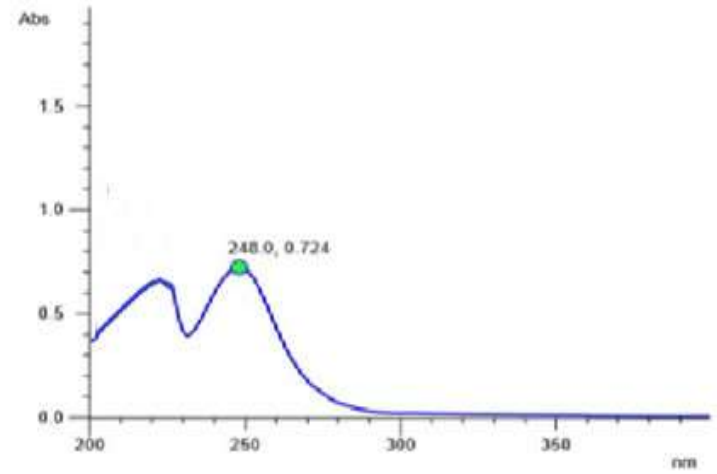

Figure 1: Determination of $\lambda_{max\ for}$ Haloperidol in phosphate buffer pH 6.8.

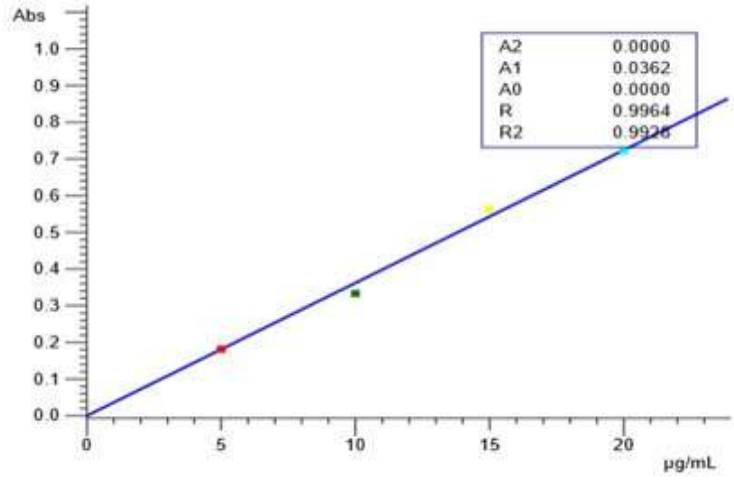

Figure 2: Calibration curve of Haloperidol in phosphate buffer pH 6.8.

Solubility study
Saturation solubility of Haloperidol in various solvents was given in Table 3.

Table 3: Results of solubility study

Solvents	Solubility (mg/ml)
Water	0.0138 ± 0.02
Methanol	15.6 ± 0.12
Propylene glycol	4.6 ± 0.04
PEG 400	3.7 ± 0.5

Since Haloperidol exhibits highest solubility in PG it was selected as a non-volatile solvent in the formulation of liquisolid compacts of Haloperidol.

Melting point

The melting point of pure samples of Haloperidol was noted as 151^{0}C which complies with the official standard of IP, indicating the purity of the sample.

Drug-Excipients compatibility studies by FT-IR

After spectral comparison, it was confirmed that there were no new peaks or disappearance of any existing characteristic peaks in case of drug when the FT-IR characterization of drug and excipients were performed. This indicates that the drug and excipients used were compatible to one another. The FT-IR spectrums for Haloperidol and physical mixture are given in Figure No.a&b. The major functional groups and corresponding wavelengths of drug Haloperidol is given in Table 4.

Table 4: Drug excipients compatibility studies by FTIR

Functional group	Wave number cm^{-1}
C=O Stretching.	1678.73
C=C Stretching.	1482.05
C-Cl Stretching.	826.27
N-H stretching.	1587.24

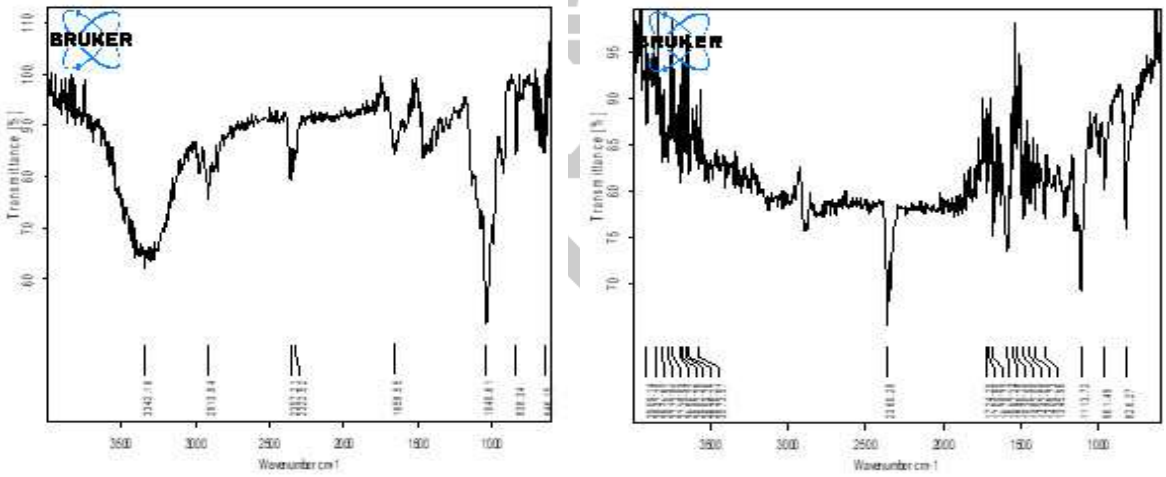

Figure 3. A) IR spectra of Haloperidol B) physical mixture.

Result of optimization of concentration of superdisintegrats.

The concentration of superdisintegrants was optimized to 7.5mg each for crospovidone and SSG in the ratio of 1:1.

Liquid load factor

Depending upon the Ø values of carrier and coating material (0.1 and 0.4 respectively) the loading factor can be calculated by using the eq.1.

The loading factors for each R value were calculated as shown in Table 5.

Table 5: Lf values for different ratios of carrier and coating material.

Carrier to Coating material ratio (R)	Liquid load factor
10	0.130
20	0.115
30	0.110
35	0.108

Results of precompression evaluations

From the results of precompression evaluation study given in Table 6 it was concluded that all the prepared batches were in the specified limits. Then the prepared powder blends were subjected to compression for formulating orodispersible liquisolid tablets.

Table 6: Precompression Parameters of liquisolid compacts

Formulation code	Bulk density (g/cc)	Tapped density(g/cc)	Carr's index	Hausner's ratio	Angle of repose(θ)
LS1	0.314±0.023	0.379±0.016	16.15±0.045	1.2±0.025	26.5±0.25
LS2	0.323±0.341	0.363±0.024	11.01±0.012	1.12±0.120	25.4±0.32
LS3	0.332±0.121	0.384±0.018	13.54±0.022	1.15±0.203	27.30±0.17
LS4	0.343±0.025	0.403±0.020	14.88±0.026	1.17±0.025	26.3±0.43
LS5	0.354±0.030	0.415±0.017	14.69±0.045	1.17±0.203	28.4±0.20
LS6	0.363±0.260	0.407±0.036	10.81±0.26	1.12±1.02	27.8±0.15
LS7	0.369±0.015	0.418±0.024	11.72±0.140	1.13±0.023	25.6±0.45
LS8	0.378±0.032	0.429±0.029	11.88±0.25	1.13±0.420	31.2±0.12
LS9	0.418±0.021	0.503±0.011	16.89±2.3	1.20±0.120	28.2±0.25
LS10	0.390±0.801	0.436±0.009	12.77±1.02	1.11±1.320	26.6±0.12
LS11	0.398±0.202	0.454±0.023	12.33±0.32	1.14±0.215	30.0±0.25
LS12	0.428±0.035	0.502±0.014	14.74±0.45	1.17±0.41	25.8±0.43

Post compression parameters

Hardness, Friability, Weight variation, Thickness, and drug content

The results of thickness, hardness, weight variation, friability and drug content of liquisolid tablets are mentioned in Table 7. None of the tested formulations had a percentage loss in tablet weights greater than 0.7 percent, indicating that all of the selected Haloperidol tablets were had acceptable friability. Mean thickness of tablets were found to be uniform in all the formulations. The thickness varied from 2.9-3.4 mm was acceptable. The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 3.0-3.6 kg/cm^2**.** The weight variation in the tablets was ranged from 0.7-1.4. Drug content was observed to vary from 93%-98%.

Table 7: Results of thickness, hardness, friability, weight variation and drug content of orodispersible Haloperidol liquisolid tablets.

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (%)	Drug content
LS1	3.4±0.023	3.6±0.052	0.229±0.120	1.2	95±0.4
LS2	3.2±0.012	3.3±0.012	0.386±0.458	0.8	98.5±0.5
LS3	3.1±0.032	3.2±0.058	0.284±0.250	1.4	98±0.8
LS4	3.3±0.120	3.3±0.078	0.453±0.59	0.9	93.5±0.3
LS5	3.2±0.056	3.1±0.150	0.721±0.025	0.7	94.5±0.6
LS6	2.8±0.058	3.3±0.025	0.626±0.012	1.1	96±0.5
LS7	3.2±0.123	3.0±0.056	0.530±0.025	1.1	95.5±0.5
LS8	2.9±0.078	3.2±0.048	0.762±0.890	0.9	95±0.2
LS9	2.8±0.59	3.1±0.045	0.326±0.170	0.9	93.5±0.8
LS10	3.1±0.091	3.5±0.069	0.650±0.045	1.1	96.5±1.0
LS11	2.9±0.258	3.4±0.045	0.408±0.025	0.9	94±0.6
LS12	3.0±0.125	3.2±0.250	0.205±0.096	0.9	93.9±0.5

Wetting time, water absorption ratio and disintegration time

The wetting time and water absorption ratio of the prepared Haloperidol liquisolid ODTs were shown in the Table 8. Wetting time was ranged from 58-85.4 sec and water absorption ratio from 62.4- 91.2%. The lesser wetting time and higher water absorption ratio was displayed by liquisolid tablets in comparison to other prepared DCTs in lab may be due to increased hydrophilicity of Haloperidol tablet as Haloperidol was converted into a liquisolid compact. The non-volatile solvents employed in liquisolid system

formulations reduce interfacial tension between the dissolution medium and the tablet/powder, making it easier to wet the final solid dosage form[21].

The disintegration time of the tablets were ranged from 25-67 sec for the prepared tablets. The faster wetting time facilitates the faster disintegration of the tablets. These results of fast disintegration can be attributed to the two superdisintegrants used crospovidone and SSG (7.5mg) in the ratio 1:1 which was optimized. Of all the 12 batches LS2 exhibited the shorter disintegration time of 25 sec.

Table.8: Results of disintegration time, wetting time and water absorption ratio of orodispersible liquisolid tablets.

Formulation code	Disintegration time (sec)	Wetting time (sec)	Water absorption ratio
LS1	38±2.5	73.5±2.0	80.0
LS2	25±1.0	58±1.6	91.2
LS3	31±1.4	62.2±2.3	83.0
LS4	34±2.0	69.8±1.3	83.6
LS5	54±1.9	80.2±3.1	70.0
LS6	35±3.0	65.3±1.2	78.0
LS7	40±1.0	74.1±1.5	75.2
LS8	42±2.0	79.3±1.9	72.0
LS9	67±1.8	96.2±2.4	60.8
LS10	44±2.1	74.5±1.4	67.2
LS11	52±2.2	80.6±2.1	65.2
LS12	55±1.9	85.4±2.6	62.4

In-vitro dissolution study

Dissolution studies were conducted for all the 12 batches (LS1-LS12), from the results it was found that LS2 formulation with a carrier to coating material ratio of 20:1 with 10% drug solution exhibited better dissolution rate (98.1%) compared to other batches.

COMPARISON OF OPTIMIZED FORMULATION OF HALOPERIDOL WITH DCT AND CONVENTIONAL MARKETED FORMULATION.

The in-vitro drug release profile of the selected formulation LS2 was first compared with the conventional marketed formulation of Haloperidol. From the results it was found that (Figure 3), liquisolid tablet formulation LS2 exhibited better dissolution profile than those of marketed conventional formulation. To confirm highest solubility was not only due to the presence of superdisintegrants, LS2 was again compared with in-vitro drug release profile of another directly compressed tablet which was prepared in the lab. From the results of comparison study, the LS2 batch had a better dissolution rate of 98.1% when compared with the DCTs (DH) of Haloperidol which was only 43.2% (Table 9). Hence it can be concluded that the increased dissolution rate of LS2 formulation may be attributed due to the adopted liquisolid technique. Another reason for the enhanced release of Haloperidol from the orodispersible liquisolid tablets may be due to the presence of non-volatile liquid vehicle (PG), where the drug still remains in dissolved state. Which aid the wettability and hence the disintegration of the prepared tablets[18]. That is the surface area of Haloperidol available in orodispersible liquisolid tablets for dissolution is much greater than that of the other directly compressed compacts.

Table 9: In-vitro dissolution profile of Haloperidol liquisolid tablet formulation LS2, DCT and marketed formulation.

Time (min)	Percentage cumulative drug release		
	LS2	DCT	Marketed product
1	56.0±0.45	15.0±1.23	20.0±1.51
2	66.5±0.96	19.7±0.96	24.5±0.99
3	71.6±0.52	24.5±0.58	28.0±0.98
5	79.0±0.25	31.5±0.85	30.7±0.85
10	84.7±0.12	36.2±0.75	37.7±0.63
15	96.2±0.32	37.7±0.52	49.5±0.53
30	98.1±0.25	43.2±0.69	64.9±0.59

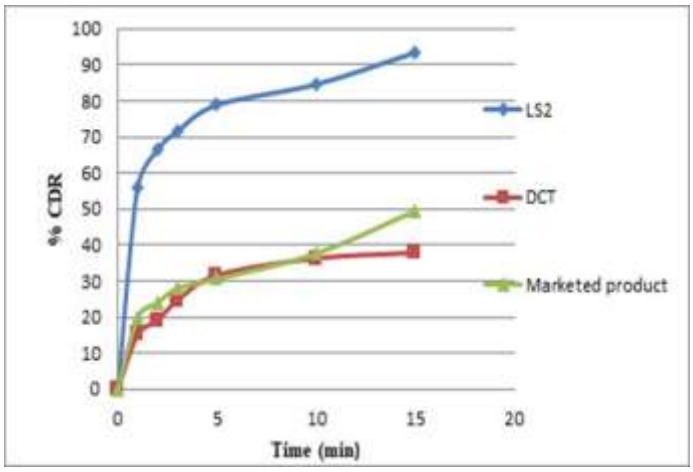

Figure No.3:In-vitro dissolution profile of Haloperidol liquisolid tablet formulation LS2 , DCT and conventional Haloperidol tablet.

SEM analysis

The shape and surface morphology of pure drug and liquisolid preparation were given in Figure 4 a,b.

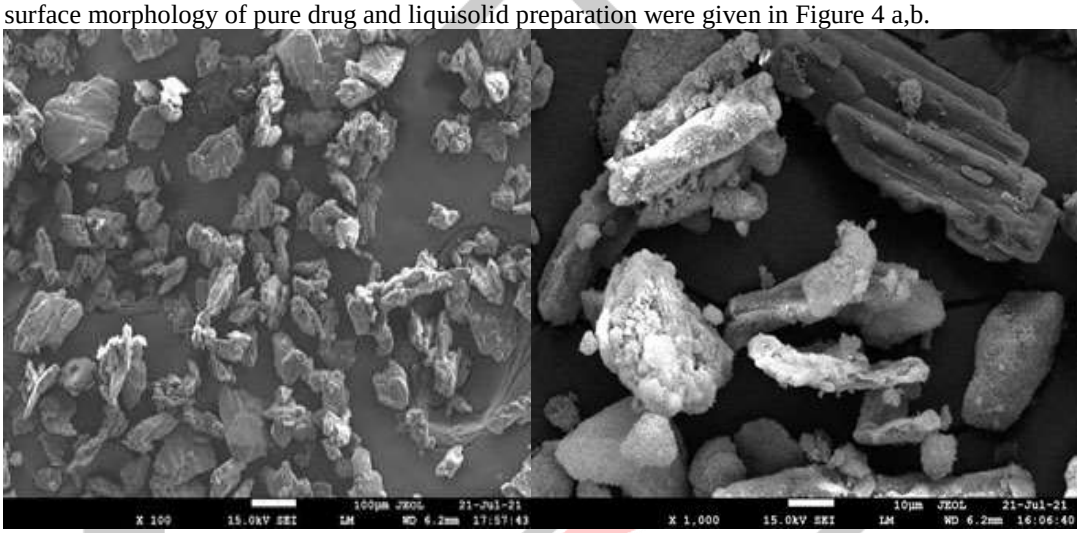

Figure 4: a) SEM of Haloperidol b) SEM of physical mixture

In SEM analysis as per Figure 4a, we can see that Haloperidol showed a crystalline nature, but when converting this pure drug into liquisolid form, the crystalline structure of the drug no more visible rather appear to be in amorphous form as in Figure 4b. Even though the compact powder appear in the solid form due to the presence of carrier and coating material added to it, the drug is actually exist in dissolved state in non-aqueous vehicle propylene glycol, that is the drug exist in a molecularly dispersed state within the powder substrate, contributing to improved drug dissolution.

Drug release kinetics

The release data obtained from the optimized formulation LS2 were fitted in to various models. The regression value (R2) was compared for zero order and first order which was found to be 0.4214 and 0.9212respectively. The R2 value of Higuchi and Hixson-Crowell were found to be 0.4982 and 0.7117 respectively. Thus we can conclude that the release kinetics follows first order, dissolution controlled pattern.

Table 10: Release kinetics of optimized formulation

Formulation code	Zero-order	First order	Higuchi model	Hixson Crowell model.
	R^2	R^2	R^2	R^2
LS2	0.4214	0.9212	0.4982	0.7117

Stability studies

Accelerated stability studies for the optimized tablet formulation LS2 were carried out at a temperature of 40 ±2 ˚C and 75±5% RH for a period of 45 days. Tablets were evaluated for physical appearance, hardness, disintegration time, wetting time, water absorption ratio, % drug content and in-vitro drug release. From the results it was seen that the tablets have not shown any significant difference during its storage period. Hence, we can conclude that tablets of LS2 batch were stable.

Conclusion

From the results obtained, it was concluded that among the 12 formulations of liquisolid orodispersible tablets prepared, the tablet formulated with 10% drug solution with carrier to coating material ratio of 20:1 (LS2) was selected as the best formulation, in terms of faster disintegration time, superior dissolution profile, and acceptable tablet properties. The comparison study showed that the tablet formulate by adopting liquisolid technique gave a far better drug release rate than that of a conventional marketed product. The enhanced dissolution rate of Haloperidol in liquisolid tablets improves the solubility and hence bioavailability of the drug.

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