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R E S E A R C H A R T I C L E

Formulation and Characterization of Amiodarone Liquisolid Compacts

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A B S T R A C T

Slow dissolution rate of poorly water soluble drugs faces major challenge in the drug development and delivery processes. Liquisolid compact technology is the most latest and novel approach for overcoming the trouble of inadequate solubility of the poorly soluble drugs. Amiodarone having poor solubility in water and used for the treatment of both supraventricular and ventricular arrhythmias. The main aim of the present study was to improve absorption efficiency and dissolution behavior of Amiodarone through Liquisolid technique. The main components of liquicompact system includes PEG 400 as solvent, Avicel PH 102 as carrier, Aerosil 200 as coating material and Cross Carmellose Sodium as disintegrant. Liquisolid compact tablets were prepared and evaluated for their tabletting properties which were found to be within the acceptable range. The prepared tablets showed good wettability, rapid disintegration and acceptable dissolution rate when compared to the marketed product. FT-IR studies revealed the there was no interaction between drug and excipients. All the formulations exhibited higher drug release when compared to marketed tablets. Hence liquisolid technique will be an easy and promising approach for enhancing the solubility and dissolution of poorly soluble drugs.

Keywords: Amiodarone, PEG 400, Avicel PH 102, Aerosil 200, Cross Carmellose Sodium, Liquisolid compact technology.

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

Oral bioavailability of a drug is greatly dependent on its aqueous solubility [1].Most of the newlydiscovered drugs have poor water solubility. In case of hydrophobic drug, dissolution is the rate limiting step, hence shows incomplete

absorption [2]. Liquisolid method is a novel technique of enhancing dissolution, which includes the conversion of liquid lipophilic or water insoluble drugs into free flowing and readily compressible powders by using a non-volatile solvent, carrier and coating materials. The drug, dissolved or suspended in non-volatile liquid vehicle (PEG 400) is incorporated into a porous carrier. Once saturation is achieved, there will be the formation of liquid layer on the particle surface which is absorbed by the coating particles. Hence, free flowing dry and compressible powder can be obtained[3].In the present study we used Aerosil 200 as coating material, Cross carmellose sodium as disintegrate and Avicel PH 102as carrier material. Amiodarone is a class-III anti-arrhythmic agent that prolong the duration of action potential but belongs to BCS class-II having poor water solubility. Hence the main aim of the present study was to enhance the dissolution rate of Amiodarone by liquisolid compact method.

2. Materials and Methods

Amiodarone was obtained from MSN laboratories, Hyderabad. Avicel PH-102and Cross povidone were provided by Yarrow chemical products, Mumbai. Polyethylene glycol-400 was provided by Sri Chandra pharmaceuticals, Hyderabad.

Pre-compression studies

Solubility studies

The Solubility studies of Amiodarone were carried out in Distilled water, PEG-200, PEG- 400, 0.1 N Hcl, Span-80, Phosphate buffer pH 7.5, Ethyl alcohol, Tween 80 and propylene Glycol for solvent selection [4]. Saturated solutions were prepared by adding excess drug to the vehicles and shaken on the vibrating shaker for 48 hrs at 25-27°C. The solution was then filtered after 48 hrs. using micron filter paper of 0.45µm and spectrophotometrically analyzed at 242 nm[5]. Results of solubility studies were shown in the Table No.2.

Drug content estimation:

Accurately weighed amount of each preparation containing 100mg of Amiodarone was dissolved in 100ml of methanol [6]. This solution was then passed through the vacuum filter and analyzed spectrophotometrically at 242 nm by using UV Visible spectrophotometer after sufficient dilution with phosphate buffer pH of 7.4[7]. Results were shown in Table-3

Flow properties:

In the production of pharmaceutical dosage forms, flow ability of a powder has greater importance, otherwise there will be more chances of dose variations[8]. The flow properties can be evaluated by Angle of repose measurements, Carr's index and Hausner's ratio.

Angle of repose:

It can be determined by the fixed funnel method. An accurately weighed powder blend was taken in a funnel and adjust the height of the funnel such that its tip was just touched the apex of the powder blend. Then the powder blend was allowed to flow through the funnel on to the surface25. The powder cone diameter was measured and angle of repose (θ) was calculated using the following equation [9].

$$\theta = \mathrm{Tan}^{-1}\, h/r$$

Where, h: height of the powder cone and r: radius of the powder cone

Bulk density:

Both bulk density (p_B) and tapped density (p_T) of formulated powder blend was determined. A fixed weight of each of the liquisolid formula were placed in a graduated cylinder and the volume occupied was measured (p_B). Then it was tapped at constant velocity up to attainment of certain volume then the volume of powder was measured (p_T)[10]

Bulk density = Weight of the powder blend/Untapped Volume of the packing

Tapped density = Weight of the powder blend/Tapped Volume of the packing

Compressibility Index: It can be determined by the formula:

Carr's Index (%) = [(TD-BD) x100]/TD

Hausner's ratio: It is the ratio of tapped density to bulk density. It was calculated from the equation:

Hausner's ratio = Tapped density/Bulk density.

Drug-exciepients interactions:

Due to drug excipient interactions in dosage forms, it became very important to check the interactions for drug and optimized formulation. FT-IR studies for Amiodarone and optimized formulations were recorded between 400 and 4000 cm^{-1} (Perkin Elmer FTIR, Perkin Elmer Inst. USA) in order to detect the drug-excipient interactions using KBr disk method. FTIR graphs shown that there is no chemical interaction between drug and excepients and it indicates that all excipients used were compatible with the drug [11].

Formulation of Amiodarone Liquisolid Compacts

Theory:

Based on the Flowable value (ø) and Compressible number (c), the quantity of excipients required were calculated. The ø value is the maximum amount of a non-volatile solvent that can be retained inside the bulk by maintaining an acceptable flowability, whereas the compressible number refers tocompactability which resulting in the compacts with sufficient hardness without any liquid leakage[12]. The liquid load factor (L_f)

$$L_f = ø + c(1/R)$$

Where ø and c are the ø values of the carrier and coating material,

R: ratio between weights of the carrier (Q) and coating material (q)

$$R = Q/q$$

The quantities of carrier (Q) and coating material (q) to be used in liquisolid system were calculated as

$Q_0 = W/L$ and $Q0 = Q_0/R$

Procedure

Required amounts of Amiodarone and solvent (PEG-400) were taken in a mortar. These contents were mixed well and incorporated into carrier (avicel pH-102) and blended thoroughly. Then the coating material (aerosil 200) was added and mixed, allow to stand for 15 minutes to allow the drug solution to be absorbed inside the powder particles and the powder on the mortar surface is scrapped off. The

disintegrant (Crosscarmellosesodium) is then added in optimum concentrations and the formulated powder was allowed to sieving for obtaining the uniform particle size which is then compressed using a rotary press [13]. Composition of Different Formulations were Shown in Table No.2.

Postcompression studies

Weight variation Test:

For estimating weight variation as per USP, 20 tablets from each formulation were randomly selected and their average weight was determined. Then individual weights were compared with average weight and observed for any deviations [14].

Friability Test:

The test was performed using Roche Friabilator in which preweighed samples of tablets were placed and subjected to 100 revolutions (for 4 min at 25 rpm). The tablets were dedusted and reweighed [15].Friability was calculated by:

$$\%Friability = (W_0\text{-}W/W_0)100$$

Where, W= final weight of tablets

W_0= Initial weight of tablets

Hardness: It indicates the ability of a tablet to withstand mechanical shocks while handling. The tablet hardness can be determined by using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly selected and their hardness was determined [16].

Disintegration test

The disintegration test was carried out in distilled water at 37 ± 2^0C using disintegration test apparatus (USP Electro lab DT) as specified in the Indian pharmacopoeia [17]

***In-vitro* Drug Release Study:** In-vitro Dissolution studies was carried out in USP Type II apparatus (Electrolab DT TDT 08L) at 50rpm in 900ml of 0.1N HCl containing 1% of Sodium lauryl sulphate (SLS) as dissolution media, and the temperature is maintained at 37±0.5ºC**.**Samples of 5 ml were withdrawn at the specified time intervals (5, 10, 15, 30, 45 and 60min) and replaced with fresh dissolution media. These samples were filtered through whatmann filter paper and analyzed spectrophotometrically at 242 nm [18].

3. Results and Discussion

Pre-compression studies

Solubility Studies:

The solubility of Amiodarone in various solvents was given in the Table No. 1shows that the Amiodarone has highest solubility in PEG-400. Hence it was chosen as solvent for dissolving the drug.

Table 2: Solubility of Amiodarone in various liquid vehicles

Solvent	Solubility (%w/w)
Propylene glycol	11
Distilled water	1.7
PEG-200	14
PEG-400	19.6
0.1 N Hcl	2.1
Tween-80	14
Glycerine	6
Span-80	9.34
Phosphate buffer 7.4	8.7
Ethyl alcohol	2.9

Drug content estimation:

The percentage drug content estimation was done for all formulations, F9 has maximum drug content of (99.5%) as shown in Table No. 3.

Table 3: Drug content estimation of Amiodarone liquisolid compacts

Formulations	Drug Content (%)
F1	92.7
F2	93.0
F3	94.9
F4	96.6
F5	95.4
F6	97.4
F7	99.2
F8	98.9
F9	99.5

Pre compression parameters:

Results of all the precompression parameters were presented in the table no. 4 which shows that all the formulations were exhibiting good flow properties.

Post compression studies: Results of post compression were tabulated for weight variation, friability, hardness and disintegration. As shown in table no.5 all the results were found to be with inacceptable limits.

***In-vitro* drug release studies:** In- vitro Drug Release Studies for formulations F1-F9 was performed and all the formulations showed more than 90% of drug release. Results of drug release were shown in the Table No. 6 and Graph No.1.

Table 4: Pre compression parameters of formulations F1-F9

Formulation	Angle of repose (in degrees)	Bulk density (g/ml.)	Tapped density(g/ml)	Carr's index (%)	Hausner's ratio
F1	34	0.345	0.571	39.57	1.655
F2	19.4	0.37	0.5441	31.99	1.47
F3	15	0.356	0.678	47.49	1.9
F4	35	0.377	0.613	38.49	1.625
F5	31	0.375	0.706	46.88	1.882
F6	24	0.308	0.761	59.52	2.47
F7	35	0.44	0.715	38.46	1.625

F8	25	0.404	0.645	37.36	1.596
F9	29	0.332	0.715	53.56	2.15

Table 5: Post compression parameters of formulations F1-F9

Formulation	Hardness (kg/cm²)	Weight Variation	Friability	Disintegration (sec)
F1	5±0.3	522±1.3	0.135±0.024	53±0.3
F2	5±0.6	545±1.4	0.152±0.025	47±0.3
F3	5±0.6	535±1.7	0.146±0.028	44±0.3
F4	5±0.4	524±1.4	0.156±0.029	43±0.2
F5	5±0.5	531±1.6	0.148±0.034	60±0.4
F6	4±0.8	533±1.3	0.168±0.031	56±0.2
F7	4±0.7	533±1.4	0.173±0.024	53±0.5
F8	4±0.6	538±1.4	0.148±0.036	48±0.4
F9	4±0.4	537±1.2	0.134±0.021	38±0.3

Table 6: *In- vitro* Drug release data of formulations F1-F9

Formulation	Cumulative percentage drug release (mean ± S.D)					
	5 min	**10 min**	**15 min**	**30 min**	**45 min**	**60 min**
F1	14±0.4	25±0.3	31±0.5	55±0.4	84±0.3	92±0.2
F2	13±0.5	22±0.2	30±0.2	51±0.5	83±0.3	90±08
F3	17±0.3	29±0.5	38±0.6	66±0.5	84±0.1	93±0.5
F4	15±0.6	27±0.3	34±0.5	64±0.4	85±0.5	95±0.1
F5	15±0.3	25±0.5	32±0.3	59±0.2	88±0.1	94±0.3
F6	18±0.4	31±0.4	42±0.6	70±0.8	88±0.3	96±0.2
F7	20±0.2	36±0.3	47±0.4	77±0.4	94±0.4	98±0.1
F8	18±0.4	37±0.4	44±0.4	75±0.6	93±0.3	97±0.5
F9	26±0.6	48±0.7	63±0.3	87±0.7	99±0.2	--

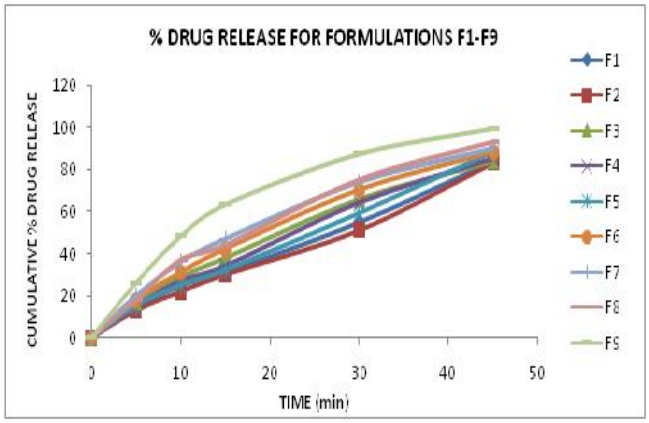

Figure 1: In- vitro Drug release data of formulations F1-F9

Among all the formulations, F9 was showing highest drug release within 45 mins due to the 30% concentration of Amiodarone in PEG-400, Avicel (90.6) and 4 % disintegrant. Formulation F9 also shows optimized results for all the evaluation parameters.

4. Conclusion

From this study we concluded that Amiodarone tablets can be formulated by using Liquisolid technique for enhancing the dissolution rate and solubility of the drug. Hence the further efficacy of prepared Liquisolid systems must be assessed by performing stability studies and pharmacokinetic studies in human beings.

5. Reference

[1] P.V. KamalaKumari, M. Trinadha Rao, Y. Srinivasa Rao, M. Aswini, Formulation and evaluation of ketoprofen liquisolid compacts, Int. J. Pharm. Sci. Rev. Res., 33(2), 2015; 45-49.

[2] Karthik Neduri, Sateesh kumar Vemula Department of Pharmaceutics, Dissolution Enhancement of Lovastatin by Liquisolid Compact Technique and Study of Effect of Carriers, 6(5), 1624-1632.

[3] Javadzadeh Y, Siahi MR, Jalali BM, Nokhodchi A,Enhancement of dissolution rate of piroxicam usingliquisolid compacts, Farmaco.60, 2005, 361–65.

[4] Nokhodchi A, Javadzadeh Y, Siahi-Shadbad MR, Barzegar-Jalali M, The effect of type and concentration of vehicles onthe dissolutionrate of a poorly soluble drug (indomethacin from liquisolid compacts, J Pharm Sci, 8, 2005, 18–25.

[5] Spireas SS, Wang T, Grover R, Effect of powder substrateon the dissolution properties of methchrothiazide liquisolid Ncompacts, Drug DevInd Pharm. 25, 1999, 163–68.

[6] Spireas S, Bolton SM, Liquisolid Systems and Methods of Preparing Same, U.S. Patent, Patent, 5, 1999, 968,550.

[7] Tayel SA, Soliman II, Louis D. Improvement of dissolutionproperties of Carbamazepinethrough

application of theliquisolid tablet technique, Eur J Pharm Biopharm, 69, 2008, 342–47.

[8] El-Gizawy SA, Effect of formulation additives in thedissolution of Meloxicam from Liquidsolid tablets, Egypt J, Biomed Sci, 25, 2007,143–58.

[9] Javadzadeh Y, Siahi MR, Asnaashari S. Nokhodchi A, Liquidsolid technique as a tool for enhancement of poorlywater-soluble drugsand evaluation of their physiochemical properties, Acta Pharm. 2007, 57, 2007, 99–109.

[10] Fahmy RH, Kassem MA, Enhancement of famotidinedissolution rate through liquisolidtablets formulation: *In-vitro and in vivo evaluation*, Eur J Pharm Biopharm, 69, 2008, 993–1003.

[11] Spireas S, Sadu S, Enhancement of prednisolone dissolutionproperties using liquisolid compacts. Int J Pharm, 166,1998, 177–88.

[12] Lin JC, Wang CY, Effects of surfactant treatment of silver powder on the rheology of its thick-film

[13] paste, Mater ChemPhys. 45, 1996, 136–44.

[14] Amidon GL, Lennernas H, Shah VP.,A theoretical basis for a biopharmaceutical classification system: The correlation of *in-vitro* drug product dissolution and in vivo bioavailability. Pharm. Res

[15] 1995,12,413-420.

[16] Sacham N K, Bhattacharya A, Pushkar S, Mishra A., Biopharmaceutical classification system: A strategic tool for oral drug delivery technology. Asian J. Pharm.2009, 3, 76–81.

[17] Anjan K Mahapatra, Murthy PN., Dissolution Enhancement & Physicochemical Characterization of Valsartan in Solid Dispersions with β-CD, HP β-CD, and PVP K-30.Dissolution technologies. 2011, 39-46.

[18] NgiikTiong, Amal A Elkordy., Effects of Liquisolid formulations on dissolution of naproxen. Eur. J. Pharm. Biopharm.2009, 73,373–384.

[19] Sheng J, Kasim N A, Chandrasekharan R, Amidon G L., Solubilization and dissolution of insoluble weak acid ketoprofen: Effects of pH combined with surfactant. Eur. J. Pharm. Sci.2006, 29,306–314.