INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND NOVEL SCIENCES

IJPRNS

FORMULATION DEVELOPMENT AND INVITRO EVALUATION OF RILUZOLE SOLID DISPERSIONS TO FAST DISSOLVING TABLETS

Y.Swathi*, Y.Nagababu, G.Rakesh, S.Manikanta, R.Naga Lakshmi, P.S.V.Aditya

Department of Pharmaceutics, JITS College of Pharmacy, Kalgampudi, Andhra Pradesh, India.

ABSTRACT

The aim of the present study is to formulate Sustained release tablets of Riluzole solid dispersions. The enhancement of oral bioavailability of poorly water soluble drugs like Riluzole could be improved by enhancing aqueous solubility. Among numerous ways of enhancing drug dissolution, solid dispersions and inclusion complexation are promising techniques to enhance the dissolution of poorly water soluble drugs. The calibration curve of Riluzole was obtained in the range of 6 to 14 µg at the wavelength of 278 nm. It has shown good linearity with a regression coefficient of 0.999 (r^2 value). This result exhibit a direct relationship between concentration of polymers and drug release. Among the various formulations tablets of batch RFD4 demonstrate of drug release (97.8%) with contains 20mg of SSG.

KEY WORDS: Riluzole, Sustained release tablets, drug release

Author for correspondence
Y.Swathi,
Department of Pharmaceutics,
JITS College of Pharmacy, Kalgampudi,
Andhra Pradesh, India.
Email id: sureshbabu3377@gmail.com

INTRODUCTION

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance. Also solid oral delivery systems do not require sterile conditions and are therefore, less expensive to manufacture. Patient compliance, high-precision dosing, and manufacturing efficiency make tablets the solid dosage form of choice. Excipients and equipments choices will be significantly affected should solid dosage form technologies change in response to the unprecedented shifts in the drug discovery such as genomics. Injections generally are not favored for use by patients unless facilitated by sophisticated auto injectors. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generate predominantly chemical entities with low molecular weights. The development of enhanced oral protein delivery technology by immediate release tablets which may release the drugs at an enhanced rate are very promising for the delivery of poorly soluble drugs high molecular weight protein and peptide. The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, manufacturing and ease of administration lead to high levels of patient compliance[8]. Many patients require quick onset of action in particular therapeutic condition and consequently immediate release of medicament is

required. It is estimated that50% of the population is affected by this problem, which results in a high incidence of ineffective therapy (1-4).

Oral route still remains the convenient route of drug administration in many diseases. But the major problem in oral drug formulations is low and erratic bioavailability, which mainly results from poor aqueous solubility of certain drugs. Incase of poorly water soluble drugs, dissolution is the rate limiting step in the process of drug absorption. So, bioavailability problems are prevalent with extremely hydrophobic drugs (aqueous solubility < 3.4 mg / ml at 37^0 C). The enhancement of oral bioavailability of poorly water soluble drugs like Riluzole could be improved by enhancing aqueous solubility. Among numerous ways of enhancing drug dissolution, solid dispersions and inclusion complexation are promising techniques to enhance the dissolution of poorly water soluble drugs. The main aim is Formulation development and invitro Evaluation of Riluzole solid dispersions to Fast dissolving tablets.

MATERIALS AND METHODS

Methods of Preparation of Solid Dispersion (5-8)

Solid dispersions were prepared by different methods like solvent evaporation and fusion method. **Solvent evaporation method-**Riluzole and each of water soluble carriers HPMC, Cyclodextrin and PEG, were weighed accurately in various ratios (1:1, 1:2 and 1:3) and transferred to beaker containing sufficient quantity of methanol to dissolve. The solvent was evaporated at room temperature. The resulting solid dispersion was stored for 24 hrs in a desiccator to congeal. Finally, dispersion were passed through sieve no.85 and stored in desiccator till further use. **Fusion Method-**Each of water soluble carrier HPMC, Cyclodextrin and PEG, were weighed accurately in various ratios (1:1, 1:2 and 1:3) and melted in a porcelain dish at 80-85ºC and to this calculated amount of Riluzole was added with thorough mixing for 1-2 minutes followed by quick cooling. The dried mass was then pulverized by passing through sieve no.85 and stored in a dessicator until used for further studies. Solid dispersions were prepared using compositions as given in Table-1 and 2.

Table-1 Composition of Riluzole solid dispersions

Solid dispersion composition	Method	Drug-Polymer ratio	Formulation Code
Riluzole: HPMC	**Solvent evaporation method**	1:1	**SD1A**
		1:2	**SD1B**
		1:3	**SD1C**
	Fusion method	1:1	**SD2A**
		1:2	**SD2B**
		1:3	**SD2C**
Riluzole: Cyclodextrin	**Solvent evaporation method**	1:1	**SD1D**
		1:2	**SD1E**
		1:3	**SD1F**
	Fusion method	1:1	**SD2D**
		1:2	**SD2E**
		1:3	**SD2F**
Riluzole: PEG	**Solvent evaporation method**	1:1	**SD1G**
		1:2	**SD1H**

		1:3	**SD1I**
	Fusion method	1:1	**SD2G**
		1:2	**SD2H**
		1:3	**SD2 I**

Table-2 Formulation Table

Ingredients (mg)	RFD1	RFD2	RFD3	RFD4	RFD5	RFD6
Riluzole SD	50	50	50	50	50	50
Cross Caramellose Sodium	10	20	-	-	-	-
Sodium Starch Glycolate	-	-	10	20	-	-
Cross Povidone	-	-	-	-	10	20
Avecil pH101	126	116	126	116	126	116
Magnesium Stearate	6	6	6	6	6	6
Talc	8	8	8	8	8	8
Total weight	200	200	200	200	200	200

***In vitro* dissolution studies**

Dissolution study was performed by using USP dissolution testing apparatus 2 (Paddle method). Weighed tablets from different batches were kept in a flask of the dissolution apparatus containing 900 ml of 1.2 pH Hcl acid buffer dissolution medium maintained at 37 ± 0.5ºC and at a speed of 50 rpm. Aliquot of dissolution medium (5 ml) was withdrawn at specific time intervals and the samples were replaced with fresh dissolution medium. Aliquot were analyzed spectrophotometrically at 278 nm against Suitable blank using UV-visible spectrophotometer.

RESULTS AND DISCUSSION

The calibration curve of Riluzole was obtained in the range of 6 to 14 µg/ml at the wavelength of 278 nm. It has shown good linearity with a regression coefficient of 0.999 (r^2 value). *In vitro* dissolution test results indicate complete dissolution of drug from all its solid dispersion within 30min figure. Among the different methods of preparation of solid dispersion, solvent evaporation method was found to be most effective. The formulation SD1F showed highest drug release within 30min. dissolution test results indicate complete dissolution of drug from all its solid dispersion within 30min figure. Among the different methods of preparation of solid dispersion, solvent evaporation method was found to be most effective. The formulation SD1F showed highest drug release within 30min. Finally, the tablets were evaluated for *in vitro* dissolution studies in simulated gastric fluid (Table-3). Formulations RFD1 demonstrate of drug release (62.4%) of having 10mg of CCS, RFD2 demonstrate of drug release (66.7%) having 20mg of CCS, RFD3 demonstrate of drug release (86.8%) which having 10mg 0f SSG showed of drug release within 15 min, RFD4 demonstrate of drug release (97.8%) with contains 20mg of SSG, RFD5 demonstrate of drug release (86.2%) with contains 10mg of CP and finally RFD6 demonstrate of drug release (92.0%) with contains 20mg of CP. Among the different formulation designs of tablets RFD4 organized with SSG 20mg which releases max. drug within 15min. and drug release. Among the various formulations tablets of batch RFD4 prepared with 20mg SSG showed complete release of drug within 15 min (Table-4 and fig-1).

Table-3 Evaluation parameters

Tablet Parameters	RFD1	RFD2	RFD3	RFD4	RFD5	RFD6
Avg. Weight (mg)	201	200	201	200	199	200
Hardness (KP)	4.2	4.5	4.6	4.2	4.1	4.4
Thickness (mm)	2.6	2.4	2.6	2.7	2.8	2.9
Disintegration(min)	3.51	3.57	3.44	3.22	3.47	3.26
Friability (%)	0.28	0.32	0.50	0.24	0.50	0.29

Table-4 Invitro drug release for the formulations

Time (mins)	RFD1	RFD2	RFD3	RFD4	RFD5	RFD6
0	**0**	**0**	**0**	**0**	**0**	**0**
5	37.4	47.2	42.9	54.8	40.4	42.1
10	48.7	56.8	67.4	79.1	64.6	71.7
15	62.4	66.7	86.8	97.8	86.2	92.0

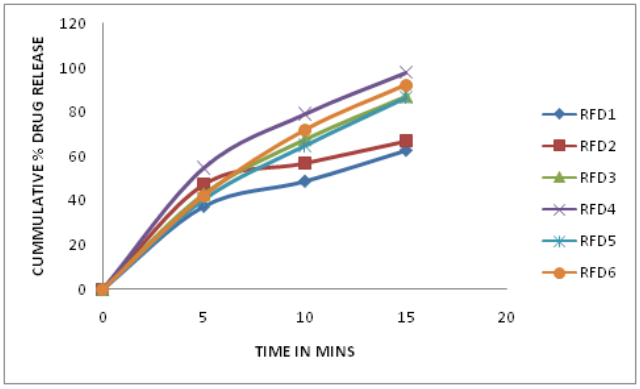

Fig-1 Graph for *in-vitro* drug release for RFD1-RFD6

CONCLUSION

Among the various solid dispersions prepared, the formulation SD1F i.e., the solid dispersion of Riluzole with Cyclodextrin prepared by solvent evaporation method shows faster dissolution rate it was decided to use formulations SD1F to formulate fast dissolving tablets using super disintegrants like CCS, sodium starch glycolate, crospovidone, by direct compression technique. The powder blend was subject to various physical characteristics tests such as bulk density, tapped density, Hausners ratio, compressibility index. The powder was compressed and the core tablets were evaluated for weight variation, hardness, thickness, disintegration time and the results were within specification. In the formulation the best results showed was with SSG 10% in formulation with Avecil pH101.

REFERENCES

1. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. *Eur J Pharm Biopharm*. 2000;50:47-60.
2. Swarbrick J, Boylan JC. *Encyclopedia of Pharmaceutical Technology*. Marcel Dekker. INC. New York. 1991;3:315.
3. Trapani G, Franco M, Latrofa A, Tullio C , Provenzano MR, Serra M, Muggironi M, Biggio G, Liso G. Dissolution properties and anticonvulsant activity of Phenytoin polyethylene glycol 6000 and polyvinylpyrrolidone K-30 solid dispersions. *Int J Pharm*, 2001;225:63-73.

4. Chiou WL, Riegelman S. Pharmaceutical applications of solid dispersion systems. *J Pharm Sci*. 1971;60(9):1281-1302.
5. Corrigan OI, Stanley T. Mechanisms of dissolution of fast release solid dispersions. *Drug Dev Ind Pharm*. 1985;11:697-724.
6. Serajuddin, ATM. Solid dispersion of poorly water soluble drugs:early promises, subsequent problems and recent breakthrough. *J. Pharm. Sci*. 1999;88(10):1058-1066.
7. Sheu MT, Yeh CM, Sokoloski TD. Characterization and dissolution of fenofibrate solid dispersion systems. *Int J Pharm*. 1994;103:137-146.
8. Tanaka N, Imai K, Okimoto K, Ueda S, lbuki YT, Higaki K and Kimura T.Development of novel sustained-release system, disintegration-controlled matrix tablet (DCMT) with solid dispersion granules of nilvadipine (II): In vivo evaluation. *J Control Rel*. 2006;122:51-56.