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ORIGINAL RESEARCH ARTICLE

Formulation and Evaluation of Immediate Release Tablets of Linezolid

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ABSTRACT

In this study Immediate Release Tablets of Linezolid were formulated by wet granulation method. Nine formulations (f2-f10) of immediate release oral tablets were prepared by using different disintegrants to get desired release profile as that of reference marketed product (f1). Evalution Parameters Like weight variation, hardness of the tablet,friability,thickness,disintegration test,drug content uniformity and in vitro release studies were performed. Formulation of linezolid having 8.0mg of HPC i.e., Formulation F-10 can be taken as an ideal or optimized formulation.

Key words: Immediate Release Tablets, Wet granulation, disintegrants, dissolution, friability, hardness.

INTRODUCTION

Tablets are the pharmaceutical solid dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding methods. They are a unit dose form, and they offer the greatest capabilities of all oral dosage forms for the greatest dose precision and the least content variability and are lightest and most compact of all oral dosage forms.Tablet may be uncoated or coated. Uncoated tablets are chewable tablet, effervescent tablet, lozenge tablet, soluble tablet, and sublingual tablet. Coated tablets are enteric coated tablet, film coated tablet, implant, sugar coated tablet, and modified-release tablet. A broken section of a coated tablet shows a core which is surrounded by a continuous layer of a different texture. There are many types of tablets like Chewable tablet, Effervescent tablet, Lozenge tablet, Soluble tablet, Sublingual tablet, Enteric coated tablet, Film coated tablet,Implant,Sugar coated tablet and Sustained release tablet. One such type of formulation is Immediate Release Tablets .Linezolid is a synthetic antibacterial agent of a new class of antibiotics, the oxazolidinones, which has clinical utility in the treatment of infections caused by aerobic Gram-positive BACTERIA.

MATERIALS USED IN THE FORMULATION

- Linezolid
- DCP dehydrate
- Light CaCO3
- HPMC
- Sodium CMC
- HPC
- Magnesium Stearate
- Colloidal SiO
- Polacrilin Potassium

Equipments Used In the Formulation Of Linezolid Tablets

- Mechanical sifter
- Rapid mixer granulator
- Multi mill
- Fluidised bed drier
- Bin blender
- Compression machine
- Dissolution apparatus
- Friability test apparatus
- Disintegration test apparatus
- Hardness tester
- Halogen moisture analyser
- Bulk tapped density apparatus(USP-I,USP-II)
- Induction cap sealer

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Plan of Work:

The present work was carried out to formulate and evaluate the immediate release tablets of Linezolid by using different binders.

I Preformulation studies

- Angle of repose
- Bulk density
- Tapped density
- Carr's Index
- Percentage compressibility
- Hausner ratio
- Analysis of Particle Size
- Moisture Content
- Drug Excipient Compatibility Studies

II. Formulation development

Evaluation of Linezolid tablets

- Weight variation
- Hardness of the tablet
- Friability
- Thickness
- Disintegration test
- Drug content uniformity
- In vitro release studies

Formulation batches:

Formulation 1 (F1):

Objective: Comparison of drug release of linezolid (form III) with linezolid (form II) of marketed formulation by using form III linezolid for marketed formulation formulae. Using same excipients and composition as in marketed formulation.

Table 1: **Formulation F-1 used in the preparation of tablets**

S.No	Ingredients	Quantity(mg)
	Intra granular	
1	Linezolid	600
2	MCC PH 101	117..6
3	Corn Starch	60
4	HPC	12
5	Purified water	q. s
	Extra granular	
6	SSG	42
7	Magnesium stearate	8.4
	Total Tablet weight	840

Table 2: Formulation table for linezolid

Formulations		F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)	F10 (mg)
Intra granular										
1	Linezolid Form (III)	600	600	600	600	600	600	600	600	600
2	Light CaCO3	60	60	60	60	60	60	60	60	60
3	Colloidal SiO_2	25	25	25	25	25	25	25	25	25
4	DCP dihydrate(di-tab) (Fujicalin)	10	10	10	10	10	10	10	10	10
5	Polacrilin Potassium	10	10	10	10	10	10	10	10	10
6	HPMC (3cps)	-	-	-	16	12	08	-	-	-
7	Sodium CMC	16	12	08	-	-	-	-	-	-
8	HPC	-	-	-	-	-	-	16	12	08
9	Purified Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Extra granular										
10	DCP dihydrate(di-tab) (Fujicalin)	82	73	69	77	78	74	77	73	74
11	Colloidal SiO_2	10	10	10	10	10	10	10	10	10
12	Polacrilin Potassium	25	25	25	25	25	25	25	25	25
13	Magnesium Stearate	10	15	15	15	10	10	15	15	10

Evaluation of immediate release linezolid tablet

Linezolid immediate release tablets was compressed under 19x8 mm capsule shaped with standard concave punch. Thicknesses, hardness, friability of the tablet were evaluated.

Table 3: Immediate release linezolid tablet evaluation table

S. No	Weight uniformity (mg)*	Thickness (mm)*	Hardness (KP)*	Disintegration Time(min)	% Friability*
F-2	841.6± 3.746	6.28± 0.016	12.6± 0.163	8.31± 0.044	0.17±0.009
F-3	843.2± 4.467	6.24± 0.020	11.8± 0.326	7.35± 0.057	0.24±0.004
F-4	840.1± 4.323	6.55± 0.016	11.8± 0.249	5.46± 0.060	0.26±0.005
F-5	840.6± 4.223	6.44 ± 0.020	12.2± 0.489	7.51± 0.016	0.17±0.007
F-6	842.7± 5.139	6.48± 0.029	12.0± 0.524	6.48± 0.028	0.22±0.009
F-7	840.9± 4.526	6.25± 0.012	12.3± 0.188	4.44± 0.057	0.17±0.009
F-8	844.7± 5.139	6.28±0.020	12.4± 0.432	7.32± 0.041	0.2 ±0.013
F-9	843.5± 5.162	6.48± 0.028	12.3± 0.188	6.31± 0.053	0.25±0.046
F-10	842.6± 4.386	6.49±0.014	12± 0.163	4.41± 0.028	0.18±0.004

*All values are expressed as Mean ± S.D, n=3

Weight variation was in range of 840.1± 4.323 to 843.5± 5.162 and hardness was in range of 11.8± 0.249 to 12.4± 0.432 .Weight variations and hardness of linezolid tablets was within range. Thickness of the tablet was in the range of 6.24± 0.020 to 6.55± 0.016mm. Length and breadth of tablets was as per the punch dimensions. Percentage friability of tablets was evaluated in 100rpm and tablets passed the friability test.

Tablet Hardness:

Hardness of tablets of each formulation was measured and found in the range of 11.8-12.6 kp. Each sample was analyzed in triplicate.

Friability:

Percentage weight loss of the tablets of each formulation was measured and found to be in the range of 0.17±0.009 to 0.26±0.005 %. Each sample was analyzed in triplicate (n = 3). Capping of tablet as not observed**.**

***In-vitro* dissolution studies:**

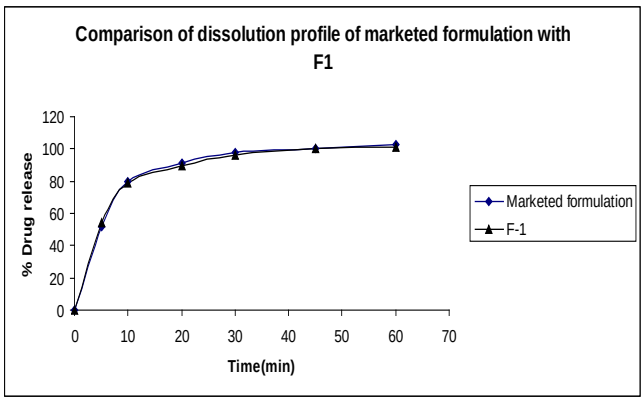
The viscosity of polymers had a dominant role as controlling factors on kinetics of drug release. As the drug is having gelling nature it will delay the release of drug to avoid for that super disintegrant polacrilin potassium is added it will avoid gel formation and drug will release immediately.

Formulation 1 (F1):

Table 4: Comparison of dissolution profile of marketed formulation with F1

Time(min)	Marketed formulation	F-1 % drug release
5	52	54
10	80	79
20	91	90
30	98	96
45	100	100
60	103	101

Fig 1: Comparison of dissolution profile of marketed formulation with F1



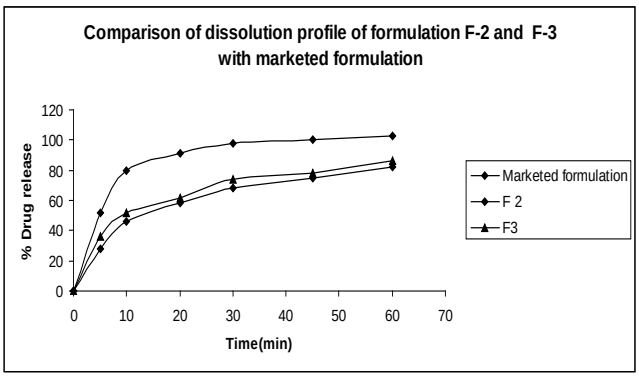
DISCUSSION

By comparing the dissolution profile of marketed formulation with form III drug, having same bioavailability as that of form II LINEZOLID, so further development can be proceeded with other excepients**.**

Table 5: Comparison of dissolution Profiles of marketed formulation with F-2 and F-3

Time(min)	Marketed formulation	F-2 % drug release	F-3 % drug release
5	52	28	36
10	80	46	52
20	91	58	62
30	98	68	74
45	100	75	78
60	103	82	86
INF	103	94	97

Fig 2: Comparison of dissolution Profiles of marketed formulation with F-2 and F-3

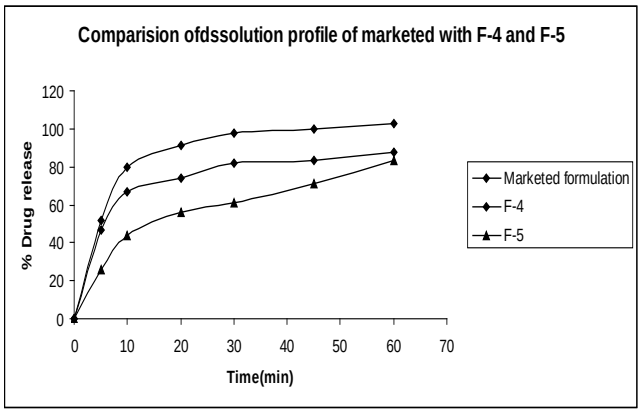


In F-2 and F-3, 16mg and12mg of sodium CMC respectively was taken to increase the drug release from linezolid tablet. But drug was released slowly compared to marketed formulation due to the gelling nature of the drug more time required to release drug compared to marketed formulation. The above release profile of linezolid tablet was much deviating from the marketed formulation. In F-4 8.0mg of sodium CMC was taken to further improve the drug release.

Table 6: Comparison of dissolution Profiles of marketed formulation with F-4 and F-5

Time (min)	Marketed formulation	F4 % drug release	F5 % drug release
5	52	47	26
10	80	67	44
20	91	74	56
30	98	82	61
45	100	83	71
60	103	88	83
INF	103	97	98

Fig 3: Comparison of dissolution Profiles of marketed formulation with F-4 and F-5

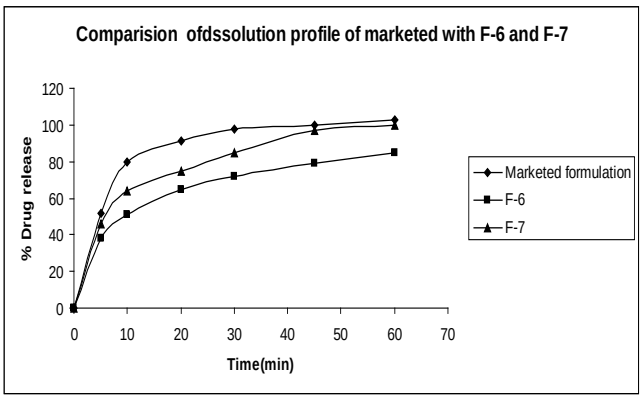


In F-4 and F-5, 8.0mg of sodium CMC and 16mg of HPMC (3cps) respectively was taken as binder to increase the drug release from linezolid tablet.
But drug was released slowly compared to marketed formulation due to the gelling nature of the drug more time required to release drug compared to marketed formulation.
The above release profile of linezolid tablet was much deviating from the marketed formulation. In F-4 drug release was further improved but drug release was very slowly compared to marketed formulation. In F-5 was taken and drug release was slow compared to marketed formulation.
The above release profile of linezolid tablet was much deviating from the marketed formulation.

Table 7: Comparison of dissolution Profiles of marketed formulation with F-6 and F-7

Time (min)	Marketed formulation	F6 % drug release	F7 % drug release
5	52	38	46
10	80	51	64
20	91	65	75
30	98	72	85
45	100	79	97
60	103	85	100
INF	103	95	103

Fig 4: Comparison of dissolution Profiles of marketed formulation with F-6 and F-7

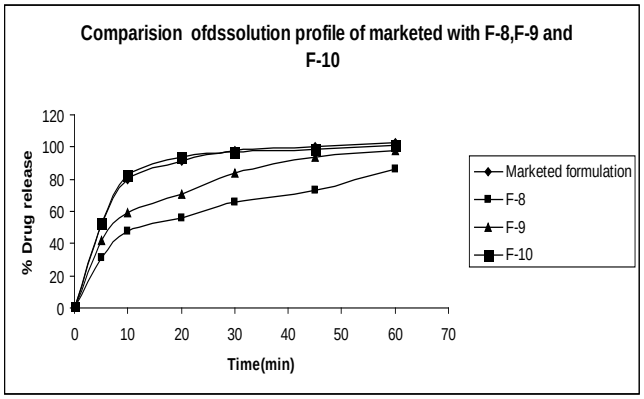


In F-6and F-7 12mg and 8.0mf of HPMC (3cps) respectively was taken as binder to increase the drug release from linezolid tablet. In the above formulation F-6 and F-7 was improved compare to previous formulations. Drug release from F-7 was much correlated to marketed formulation.
To check the effect of HPC on drug release and to obtain the dissolution profile similar to that of marketed formulation further trials was carried out with HPC.

Table 8: Comparison of dissolution Profiles of marketed formulation with F-8, F-9 and F-10.

Time (min)	Marketed formulation	F-8 % drug release	F-9 % drug release	F-10 % drug release
5	52	31	42	53
10	80	48	59	82
20	91	56	71	94
30	98	66	84	97
45	100	73	94	99
60	103	86	98	101
INF	103	101	101	103

Fig 5: Comparison of dissolution Profiles of marketed Formulation with F-8,F-9 and F-10



In Formulations F-8, F-9 and F-10 HPC was taken at 16, 12 and 8mg. respectively was taken as binder to increase the drug release from linezolid tablet. In the above formulation F-8 and F-9 was showing faster release profile but F-10 was showing better release profile which was correlating with marketed formulation.

CONCLUSION

This study discusses the preparation of immediate release tablets of Linezolid
Immediate release tablets of linezolid were prepared by wet granulation method. All the

formulated tablets met the pharmacopoeia standard of uniformity of weight, percentage friability, thickness and hardness.

The behavior of all formulated tablets was found, because all formulations contain similar composition of different binders. During the optimization of formulation it was observed in dissolution that decreasing the concentration of binder increasing release profile could be achieved. It was also observed that dissolution is highly dependent on the hardness (density) of tablet.

The in-vitro dissolution study was carried out by using USP Type-1 dissolution apparatus. In formulation F1 behavior of Form III linezolid is compared with marketed formulation of linezolid form II and it was observed that form III linezolid was correlating with the release profile of form II of marketed formulation. Formulations F2 to F10 showed that as we increase the concentration of binder drug release decreases significantly.

From the above results and discussion it is concluded that formulations F2, F3, F4, F5, F6, F8 and F9, showed that release profile which was not correlating with marketed formulation. From the in-vitro release profile of formulations F7 and F10 having similar release profile as marketed formulation. But initially in F7 drug release is less as compared to marketed formulation and in F10 formulation it was matching with marketed formulation. Formulation of linezolid having 8.0mg of HPC i.e., Formulation F-10 can be taken as an ideal or optimized formulation.

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