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Formulation and Evaluation of Niacin Extended Release Tablets

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A B S T R A C T

The objective of the present work was to develop extended release tablets of Niacin using various grades of Eudragit polymers and Film forming agents like Surelease, Kollicoat SR 30D, Eudragit RL 100 either alone or in combination. Tablets were prepared by Wet Granulation method. The different excipients were tested for their compatibility with the drug by using FTIR Studies which revealed that there was no interaction. The Pre-compression parameters such as bulk density, tapped density, Compressibility index and hausner ratio were analyzed for the prepared tablet blend were found to be satisfactory. The Post-compression parameters such as thickness, hardness, friability, weight variation, drug content uniformity were evaluated for core tablets and they were within the pharmacopoeial limits. The *in-vitro* drug release studies were performed in USP Apparatus I (Basket). Among the formulations F11E showed drug release for 24 hrs with cumulative percentage of 98.9 similar to that of Innovator. The kinetic treatment showed that the optimized formulation followed Korsemeyer-peppas with release exponent (n) 0.759. The results indicated that the selected formulation was stable during stability studies. The formulation F11E showed diffusion coupled with erosion mechanism of drug release.

Keywords: Extended release, Eudragit polymers, Wet Granulation, Korsemeyer-peppas, diffusion, Erosion.

A R T I C L E I N F O

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1. Introduction

Modified Drug Delivery:

The term modified-release product is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified release form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments or promptly dissolving dosage forms as presently recognized" [**1].**

Modified drug delivery systems are divided into four categories[2]**.**

A. Delayed release
B. Extended release
C. Site specifying targeting
D. Receptor targeting

A. Delayed Release:

These systems are those that use repetitive, intermittent dosing of a drug from one or more immediate release units incorporated into a single dosage form. Examples of delayed release systems included repeat action tablets, capsules and enteric-coated tablets where timed release is achieved by a barrier coating.

B. Extended Release:

These system are includes any dosage form that maintains therapeutic blood or tissue levels of the drug for a prolonged period. It is considered as a controlled drug delivery system.

C. Site specific targeting:

These systems refer to targeting of a drug to a certain biological location. In this case the target is adjacent to the effected organ or tissue.

D. Receptor targeting:

These systems refer to targeting of a particular drug receptor within an organ or tissue.

Site specific targeting and receptor targeting systems satisfy the spatial aspect of drug delivery and are also considered to be controlled drug delivery systems.

Potential Advantages of Extended Release Drug Therapy [2, 3,4]:

All extended release products share the common goal of improving drug therapy over that achieved with their non-controlled counter parts. This improvement in drug therapy is represented by several potential advantages of use of extended release systems are:

i. Avoid patient compliance problems.

ii. Employ less total drug

- Minimize or eliminate local side effects.
- Minimize or eliminate systemic side effects.
- Obtain less potentiation or reduction in drug activity with chronic use.
- Minimize drug accumulation with chronic dosing.

iii. Improve efficiency in treatment

- Cure or control condition more promptly
- Reduce fluctuation in drug level
- Improve bioavailability of some drugs
- Make use of special effects e.g., extended release aspirin for morning relief of arthritis by dosing before bedtime [5,6].

2. Materials and Methods

Table 1: Composition of Niacin Extended Release tablets 1000 mg tablet

Ingredients (Mg/tab)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**
Niacin	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000	1000
Avicel PH101	209	144	79	209	144	79	176.5	76.5	44	76.5	44
Eudragit RL 30D	65 (5%)	130 (10%)	195 (15%)	-	-	-	-	-	-	-	-
Eudragit RS 100	_	_	_	65 (5%)	130 (10%)	195 (15%)	_	_	_	_	_
Eudragit RS PO	-	-	-	-	-	-	65 (5%)	65 (5%)	65 (5%)	65 (5%)	65 (5%)
Povidone K-30	_	_	_	_	_	_	32.5 (2.5%)	32.5 (2.5%)	65 (5%)		
Povidone K-90	_	_	_	_	_	_	_	_	_	32.5 (2.5%)	65 (5%)
Aerosil	13	13	13	13	13	13	13	13	13	13	13
Magnesium Sterate	13	13	13	13	13	13	13	13	13	13	13
Dicalcium Phosphate Dihydrate	_	_	_	_	_	_	_	100	100	100	100
Acetone	-	-	-	Qs	Qs	Qs		-	-	-	-
Isopropyl Alcohol				Qs	Qs	Qs		_	_	_	_
Water	Qs	Qs	Qs				Qs	Qs	Qs	Qs	Qs
Total	**1300**	**1300**	**1300**	**1300**	**1300**	**1300**	**1300**	**1300**	**1300**	**1300**	**1300**

Coating of F11 Tablets (F11A – F11E); *F11 E is OPTIMIZED BATCH

3. Results and Discussion

Table 2: Standard graph of Niacin

Conc (µg/ml)	Absorbance
0	0
5	0.15418
10	0.33262
15	0.50294
20	0.66784
25	0.84093

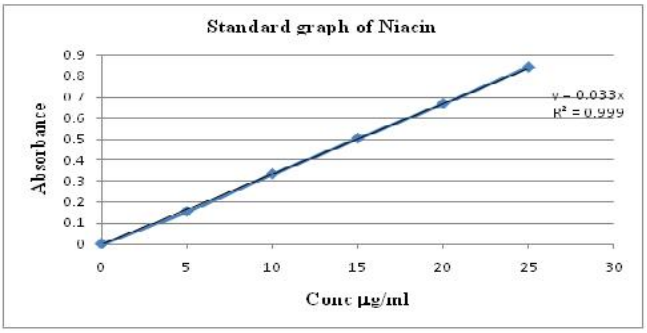

Figure1: Standard Graph of Niacin

Pre-Compression Parameters:

The physical properties like Angle of Repose, Bulk density, Tap density, Carr's Compressibility Index and Hausner ratio are given in the following table.

Table 3: Physical properties of granules

Formulation Code	Angle of Repose	Bulk Density (gm/ml)	Tap Density (gm/ml)	Carr's Compressibility Index (%)	Hausner's Ratio
F1	24^0 35'	0.520	0.625	16.66	1.20
F2	26^0 15'	0.510	0.625	18.36	1.23
F3	23^0 12'	0.512	0.643	20.40	1.26
F4	25^0 19'	0.520	0.625	16.66	1.20
F5	28^0 26'	0.425	0.540	21.27	1.27
F6	24^0 13'	0.439	0.532	17.54	1.21
F7	26^0 18'	0.425	0.543	21.32	1.28
F8	27^0 45'	0.370	0.512	27.77	1.38
F9	25^0 57'	0.392	0.526	25.49	1.34
F10	24^0 14'	0.400	0.500	20.00	1.25
F11	$24^0$36'	0.480	0.595	17.30	1.24

Post Compression Parameters

Table 4: Physical parameters of 1000 mg ER tablets

Formulation Code	Weight Variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)
F11A	1314 ± 1.160	11.31 ± 0.437	8.12 ± 0.221	0.14
F11B	1315 ± 1.196	11.18 ± 0.295	8.13 ± 0.334	0.13
F11C	1332 ± 1.657	11.40 ± 0.147	8.17 ± 0.214	0.16
F11D	1320 ± 1.963	11.36 ± 0.143	8.13 ± 0.234	0.14
F11E	1330 ± 1.661	11.45 ± 0.147	8.16 ± 0.234	0.13

In-Vitro Dissolution Study

Table 5: Cumulative Percentage of drug release from 1000 mg ER tablets F11

Sampling Time (hrs)	Cumulative % Drug Release (mean ± SD) (n=3)	
	Innovator	F11
1	9.3 ± 0.316	16.9 ± 0.48
3	18.6 ± 1.181	31.3 ± 0.94
6	36.9 ± 1.288	42.9 ± 0.88
9	48.6 ± 0.440	53.5 ± 0.83
12	61.9 ± 1.190	67.4 ± 0.18
15	72.3 ± 1.969	78.2 ± 0.65
20	85.5 ± 0.220	89.6 ± 0.38
24	98.6 ± 0.494	98.6 ± 0.61

Table 6: Mathematically modeling and drug release kinetics

Formulations	Drug release kinetics (R^2)				
	Zero order	First order	Higuchi	Korsemeyer	Release exponent (n)
F1	0.898	0.964	0.996	0.997	0.462
F2	0.919	0.968	0.978	0.995	0.456
F3	0.929	0.904	0.981	0.994	0.471
F4	0.868	0.989	0.990	0.991	0.482
F5	0.873	0.973	0.992	0.994	0.478
F6	0.876	0.964	0.993	0.995	0.480
F7	0.915	0.919	0.994	0.996	0.563
F11	0.950	0.876	0.993	0.996	0.561
F11A	0.988	0.986	0.903	0.992	0.514
F11B	0.926	0.994	0.993	0.995	0.618
F11C	0.888	0.881	0.955	0.958	0.707
F11D	0.966	0.845	0.985	0.997	0.652
F11E	0.971	0.832	0.978	0.997	0.759
Innovator	0.978	0.828	0.974	0.995	0.762

The release kinetics, dissolution rate, process variables such as hardness, weight variation during granulation are the some factors found critical during the development based on the experimental finding. Preformulation studies were done initially and results directed the further course of formulation. With the data literature review, Preformulation and prototype formulation trails were started. Wet granulation method was formulation. Granules were evaluated for tests such as bulk density, Tapped density, Compressibility Index and Hausner ratio before being punched as tablets. Tablets were tested for weight variation, thickness and friability, in-vitro dissolution tests were performed and percentage drug release was calculated. Dissolution tests were performed and percentage drug release was calculated.

4. Conclusion

Dissolution profile of Formulation -11E matched with that of Innovator's (NIASPAN) product. In the dissolution modeling all the developed formulations followed Korsemeyer-peppas drug release. The optimized formulation F11E followed Korsemeyer-peppas drug release drug release and non-Fickian model. The developed formulation was tested for its stability for three months and found to be stable. In the present study, polymethacrylates were found to play a great role in controlling release of drug niacin from the matrix system. Accordingly, it can be concluded that the formulation is robust in the performance is less likely to be affected by the various factors studied. An excellent invitro correlation is expected and is evident from the degree of similarity found in dissolution and release kinetics with respect to the innovator's product, Niaspan.

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