World Inventia Publishers

Journal of Pharma Research

http://www.jprinfo.com/

Vol. 7, Issue 6, 2018 ISSN: 2319-5622 USA CODEN: JPROK3

Research Article

FORMULATION AND EVALUATION OF FLOATING AND MUCOADHESIVE TABLET OF ORAL HYPOGLYCEMIC DRUG OF NATEGLINIDE

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Received on: 02-06-2018; Revised and Accepted on: 17-06-2018

ABSTRACT

In the present research work gastro retentive mucoadhesive floating formulation of Nateglinide by using various hydrophilic polymers. Nateglinide is a drug for the treatment of type 2 diabetes. Initially analytical method development was done for the drug molecule (1-4). Absorption maxima was determined based on that calibration curve was developed by using different concentrations. Gas generating agent accrual and bioadhesive polymer carbopol concentration was optimized. Twelve formulations were developed by using different concentrations of polymers of various polymers. The formulation blend was subjected to various preformualation studies (5-8), flow properties and all the formulations were found to be good indicating that the powder blend has good flow properties. The prepared tablets were evaluated, by invitro dissolution test results it was found that formulation F12 prepared by using HPMC K15 M and HPMC k 100 M has shown the maximum drug release hence it was considered as the optimized formulation. The optimized formulation dissolution data was subjected to release kinetics (9-10), from the release kinetics data it was evident that the formulation followed zero order kinetics of drug release.

KEYWORDS: *Nateglinide, Preformualation, Hydrophilic Polymers.*

INTRODUCTION

Nateglinide (trade name **Starlix**) is a drug for the treatment of type 2 diabetes. Nateglinide was developed by Ajinomoto, a Japanese company and sold by the Swiss pharmaceutical company Novartis. Nateglinide belongs to the meglitinide class of blood glucose-lowering drugs.

The oral route is increasingly being used for the delivery of therapeutic agents because the low cost of the therapy and ease of administration lead to high levels of patient compliance [1-3]. More than 50%of the drug delivery systems available in the market are oral drug delivery systems1. Controlled-release drug delivery systems (CRDDS) [4-6] provide drug release at a predetermined.

MATERIALS AND METHODS

Experimental Procedure:
Drug Profile:
Drug name: Nateglinide

IUPAC name: (2R)-3-phenyl-2-{[4-(propan-2-yl)cyclohexyl]formamido} propanoic acid

Solubility: Soluble in ethanol practically insoluble in water

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DOI: https://doi.org/10.5281/zenodo.1291615

Molecular Formula: $C_{19}H_{27}NO_3$

Molecular Weight: 317.4226

Bioavailability: 73%

Half-life: 1 .5 hours

Protein binding: 98% bound to serum proteins, primarily serum albumin and to a lesser extent α1 acid glycoprotein

Dosage forms: Tablet

Dose: 60mg, 120mg

Category: Hypoglycemic Agents, Meglitinides

Pharmacokinetic Properties:
Absorption:

Rapidly absorbed following oral administration prior to a meal, absolute bioavailability is estimated to be approximately 73%. Peak plasma concentrations generally occur within 1 hour of oral administration. Onset of action is <20 minutes and the duration of action is approximately 4 hours.

Distribution:

Nateglinide protein binding is 98% (primarily albumin, and to a lesser extent to alpha-1 acid glycoprotein). Vd is 10 L (IV).

Metabolism:

Hydroxylation followed by glucuronide conjugation via CYP2C9 (70%) and CYP3A4 (30%).

Elimination:

Nateglinide is eliminated in urine (83% as metabolites, 16% as parent compound) and feces (10%). The half-life is 1.5 h.

Adverse Effects: Accidental trauma, dizziness, abdominal pain, dyspepsia, arthropathy.

Storage: Store at room temperature at 77 degrees F (25 degrees C) away from light and moisture. Brief storage at 59-86 degrees F (15-30 degrees C) is permitted.

Methodology:

Formulation development of Nateglinide Tablets:

All the formulations were prepared by direct compression [10-13]. The compression of different formulations are given in Table I .The tablets were prepared as per the procedure given below and aim is to prolong the release of Nateglinide. Total weight of the tablet was considered as 500mg.

Procedure:

1) Metformin and all other ingredients were individually passed through sieve no ≠ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method.

RESULTS AND DISCUSSION

The present study was aimed to developing gastro retentive floating tablets of Nateglinide using various polymers. All the formulations were evaluated for physicochemical properties and invitro drug release studies.

Analytical Method:

Graphs of Nateglinide were taken in Simulated Gastric fluid (pH 1.2) at 234 nm.

Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the tablets.

Table No. 1: Formulation development of Nateglinide Tablets

S. No.	Excipient Name	EF1	EF2	EF3
1	Nateglinide	60	60	60
2	HPMCK 4M	120	120	120
4	Carbopol 934P	50	50	50
5	Accrual	30	60	90
5	Mg.Stearate	5	5	5
6	Talc	5	5	5
7	MCC pH 102	Q.S	Q.S	Q.S
	Total weight	500	500	500

All the quantities were in mg.

Table No. 2: Formulation composition for floating tablets

Formulation No.	Nateglinide	HPMC K4M	HPMC K15M	HPMC K100M	Accural	Carbopol 934P	Carbopol 971P	Mag. Stearate	Talc	MCC pH 102
F1	60	60	-----	-----	60	50	50	5	5	QS
F2	60	120	-----	-----	60	50	50	5	5	QS
F3	60	180	-----	-----	60	50	50	5	5	QS
F4	60	-----	60	-----	60	50	50	5	5	QS
F5	60	-----	120	-----	60	50	50	5	5	QS
F6	60	-----	180	-----	60	50	50	5	5	QS
F7	60	-----	-----	60	60	50	50	5	5	QS
F8	60	-----	-----	120	60	50	50	5	5	QS
F9	60	-----	-----	180	60	50	50	5	5	QS
F10	60	60	-----	60	60	50	50	5	5	QS
F11	60	60	60	-----	60	50	50	5	5	QS
F12	60	-----	60	60	60	50	50	5	5	QS

All the quantities were in mg, Total weight is 500 mg.

Table No. 3: Observations for graph of Nateglinide in 0.1N HCl (234 nm)

concentration	Absorbance
0	0
0.5	0.173
1	0.346
1.5	0.475
2	0.647
2.5	0.823

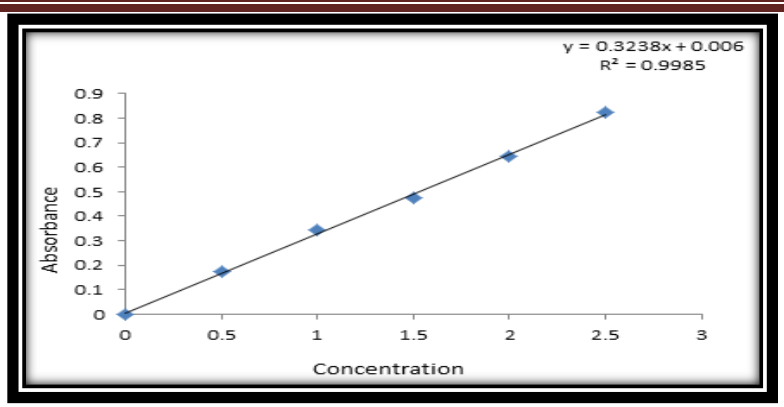

Fig. 1: Standard graph of Nateglinide in 0.1N HCl

Table No. 4: Preformulation parameters of powder blend

Formulation Code	Bulk Density (gm/cm²)	Tap Density (gm/cm²)	Carr's Index (%)	Hausner ratio	Angle Of Repose(Θ)
F1	0.45±0.09	0.55±0.95	18.18±0.10	1.22±0.37	27.91±0.03
F2	0.47±0.12	0.55±0.46	14.54±0.05	1.17±0.82	28.23±0.10
F3	0.50±0.19	0.58±0.43	13.79±0.07	1.16±0.52	29.34±0.18
F4	0.46±0.53	0.55±0.56	16.36±0.04	1.19±0.63	26.71±0.13
F5	0.50±0.55	0.58±0.53	13.79±0.28	1.16±0.08	29.34±0.17
F6	0.47±0.05	0.55±0.63	14.54±0.37	1.17±0.06	28.23±0.22
F7	0.50±0.07	0.58±0.37	13.79±0.44	1.16±0.10	29.34±0.63
F8	0.41±0.67	0.50±0.28	18±0.47	1.21±0.38	26.78±0.38

Table No. 5: Quality control parameters for tablets

Formulation code	Weight variation (mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (min)
F1	505	3.5	0.43	3.59	97.23	4.3
F2	504	3.6	0.34	3.64	98.55	4.9
F3	510	3.5	0.49	3.59	98.16	4.1
F4	509	3.6	0.47	3.58	99.34	4.5
F5	499.4	3.3	0.49	3.59	98.16	3.9
F6	502	3.7	0.34	3.64	98.55	4.2
F7	501	3.5	0.49	3.59	98.16	4.1
F8	507	3.6	0.34	3.56	99.25	3.9
F9	502	3.5	0.34	3.56	99.25	4.2
F10	503	3.4	0.43	3.55	98.6	4.6
F11	502.4	3.8	0.54	3.45	98.7	4.5
F12	498.5	3.5	0.43	3.54	98.5	4.1

***In-Vitro* Drug Release Studies:**

Table No. 6: Dissolution Data of Nateglinide Tablets

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	3.77	9.14	5.12	6.75	8.11	5.18	8.21	8.23	5.54	3.11	10.37	15.38
1	10.51	16.76	12.45	12.34	14.5	11.81	22.8	17.55	12.17	7.15	21.11	27.77
2	18.4	25.77	17.47	24.88	20.82	21.27	27.21	22.42	24.58	14.21	31.55	36.44
3	24.15	29.42	23.42	31.55	26.89	25.43	38.11	28.11	33.19	27.54	35.68	43.77
4	32.13	34.64	29.18	38.76	34.14	37.51	41.47	36.67	39.79	35.45	39.77	47.59
5	37.91	41.32	36.71	42.44	41.67	43.14	47.65	48.71	48.69	45.21	43.28	49.85
6	42.92	49.12	41.78	45.89	47.64	47.15	51.58	56.86	52.75	53.77	47.77	54.66
7	48.18	54.77	48.89	48.59	58.66	51.79	56.34	59.49	61.38	59.34	49.86	64.01
8	54.32	58.74	52.22	53.55	63.77	53.14	61.12	64.46	67.54	66.73	52.37	75.77
9	59.93	64.4	58.42	59.87	76.52	63.18	67.48	69.19	75.28	77.69	56.61	77.55
10	64.82	77.31	63.34	62	83.76	68.14	69.49	73.42	85.19	85.54	62.44	79.55
11	69.77	85.12	69.42	74.66	88.15	74.19	77.27	81.12	91.14	91.15	69.55	84.65
12	78.22	89.21	77.47	78.55	94.36	83.45	86.59	86.41	93.68	97.05	75.33	87.54

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How to cite this article:

G. Jagadish, Dr. Anil Kumar Middha. FORMULATION AND EVALUATION OF FLOATING AND MUCOADHESIVE TABLET OF ORAL HYPOGLYCEMIC DRUG OF NATEGLINIDE. J Pharm Res 2018;7(6):109-112. **DOI: https://doi.org/10.5281/zenodo.1291615**

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil