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FORMULATION AND EVALUATION OF NATEGLINIDE SR TABLETS

N. Sony Priyanka*, Ch. Buddeswara Rao, J. Hima Iswarya, K. G. N. S. Kamalesh, K. Mounika, K. Harshitha, K. Kasturi
Department of Pharmaceutics, JITS College of Pharmacy, Kalgampudi, Andhra Pradesh, India.

ABSTRACT
Matrix tablets were compressed without any problem and do not require any change in ratio of excipients in formulation. Results of the present study demonstrated that natural polymers could be successfully employed for formulating sustained-release matrix tablets ofNateglinide. The release of drug depends not only on the nature of matrix but also upon the concentration of polymer. As the percentage of polymer increased, the rate of release decreased. The formulation F6 was optimized because drug release was sustained up to 12hrs.
Key Words: Nateglinide, Matrix tablets, optimized drug release

Author for correspondence
N. Sony Priyanka,
Department of Pharmaceutics,
JITS College of Pharmacy, Kalgampudi, Andhra Pradesh, India.
Email id: leelasiddardha@gmail.com

INTRODUCTION
A solid dosage form is drug delivery system that includes tablets, capsules, sachets and pills as well as a bulk or unit-dose powders and granules. Among the various dosage forms oral soliddosage forms have greater importance and occupy a prime role in the pharmaceutical market. Widely acceptable route of administration is said to be orally and the drugs that administered through oral route as solid dosage forms were known to be most preferred ones by the patients. 90% of the drugs which shows systemic effect were formulated as solid dosage forms. Because of these reason whenever New chemical entity (NCE) has discovered, which shows a sufficient pharmacological action, first the pharmaceutical company asks whether the drug is successfully administered by oral route or not. The oral route of administration still continues to be the most preferred route due to its manifold advantages including:Tablets and capsules represent unit dosage forms in which the accurate dose of drug to show sufficient pharmacological action can be administered. In case of liquid oral dosage forms such as Syrups, Suspensions, Emulsions, Solutions and Elixirs the patient is asked to administer the medication of 5-30 ml. Such dosage measurements are typically error by factor ranging from 20-50 %, when the drug is self-administered by patient.Solid dosage forms are less expensive to shipping and less prone for the degradation when compared to liquid dosage forms.In 1843, the first patent for a hand operated device used to form a tablet was granted." Tablets are defined as solid preparations each containing a single dose of one or more active ingredients and obtained by compressing uniform volumes of particles. They are intended for oral administration, some are tablets to be swallowed with a drink of water, and some are chewable. Dispersed tablets need to be dispersed in water before administration, and some tablets should kept on the mouth then the liberation of active

ingredient takes place. Tablets are the preferred ones when the drug need systemic drug delivery and also for local drug action. For systemic use drug must be formulated in the form of a tablet of which it needs fluids for its dissolution as they pass through mouth, stomach and intestine and then absorbed into systemic circulation to reach its site of action. Tablets are the most desired solid unit dosage forms because of it advantages tothe manufacturers [e.g. simplicity and economy of preparation, stability and convenience in packing, shipping and dispensing] and the patient [e.g. accuracy of dosage, compactness, portability, blandness of taste and ease of administration].The size and weight of the tablets may vary of its drug amount and intended method of administration (1-4). The present work is aimed at preparing and evaluating sustained-release (SR) matrix tablets of Nateglinide using different polymers.

MATERIALS AND METHODS

Preparation of Nateglinide Matrix Tablets

All the matrix tablets, each containing 120mg of Nateglinide, were prepared by direct compression method. Direct compression- Accurately weighed amounts of drug, polymer,binder and diluent were mixed geometrically in a mortar. This mixture was passed through No.40 sieve and thoroughly mixed in a polythene bag for 15 minutes. The powder blend was then lubricated with magnesium stearate and Talc for 2 minutes and compressed into tablets on a 16-station rotary tableting machine using 9mmround, flat-faced punches.The drug polymer ratio was developed to adjust drug release as per theoretical release profile and to keep total weight of tablet constant for all the fabricated batches under experimental conditions of preparations. The total weight of the matrix tablets was 300mg with different drug polymer ratios. The various polymers used were HPMCK4M, Ethyl cellulose and HPMCK100M. Fillers like Micro crystalline cellulose lubricants like magnesium stearate and talc were used for the preparation of matrix tablets (Table-1).

Table-1 Composition of Matrix Tablets Containing Nateglinide sustained release tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Nateglinide	120	120	120	120	120	120	120	120	120	120	120	120
PVPK30	15	15	15	15	15	15	15	15	15	15	15	15
HPMCK4M	45	60	75	--	--	--	--	--	--	30	--	30
HPMCK100M	--	--	--	--	--	--	45	60	75	--	30	30
Ethyl cellulose	--	--	--	45	60	75	--	--	--	30	30	--
MCC	116	101	86	116	101	86	116	101	86	101	101	101
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Mg.stearate	2	2	2	2	2	2	2	2	2	2	2	2
Total weight	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**

In -Vitro Drug Release Characteristics

Drug release was assessed by dissolution test under the following conditions: n = 3, USP type II dissolution apparatus (paddle method) at 50 rpm in 900 mL of 0.01N HCl for first 2 hours and the phosphate buffer pH 6.8 from 3 to 12 hours, maintained at 37°C ± 0.5°C. An aliquot (5mL) was withdrawn at specific time intervals and replaced with the same volume of pre warmed (37°C ± 0.5°C) fresh dissolution medium. The samples withdrawn were filtered through Whatmann filter paper (No.1) and drug content in each sample was analyzed by UV-visible spectrophotometer at 210 nm (5, 6).

RESULTS AND DISCUSSION

The values obtained for angle of repose for all (F_1-F_{12}) formulations are tabulated inTable-2. The values were found to be in the range from 27^0.36′- 29^0.69’. This very good flow property of the powdered blend. The values obtained for compressibility index for all (F_1-F_{12}) formulations are tabulated in Table-2 Compressibility index value ranges between 12.23%-17.50±0.8% indicating that the blend have the required flow property for compression. The values obtained for hausner’s ratio for all (F_1-F_6) formulations are in Table-2 Hausner’s ratio value ranges between1.11-1.21 indicating that the powdered blend have the required flow property for compression.

Table-2 post compression parameters

Formulation code	Thickness ± S.D. (mm) n = 3	Hardness ± S.D. (KP) n = 3	Friability (%)	Average weight variation (mg) n = 3	Drug content (%) n = 3
F1	2.58±0.09	6.9±0.35	0.13	298±0.19	99.5±0.16
F2	2.57±0.04	6.6±0.29	0.25	297±0.24	98.3±0.65
F3	2.54±0.07	6.85±0.32	0.31	302±0.17	97±0.54
F4	2.56±0.10	6.67±0.25	0.11	298±0.20	97±0.56
F5	2.59±0.08	6.5±0.56	0.23	298±0.28	98.5±0.45
F6	2.58±0.05	6.9±0.22	0.23	297±0.25	99.8±0.67
F7	2.57±0.05	6.9±0.39	0.13	299±0.14	99.9±0.13
F8	2.53±0.04	6.6±0.27	0.26	298±0.25	98.8±0.64
F9	2.52±0.07	6.8±0.34	0.35	307±0.16	97.7±0.56
F10	2.59±0.10	6.68±0.22	0.14	296±0.27	97.6±0.57
F11	2.59±0.09	6.51±0.50	0.24	295±0.29	98.5±0.48
F12	2.58±0.07	6.8±0.28	0.22	297±0.28	99.4±0.69

From results it was confirmed that the except F6 remaining all formulations does not fulfill the sustained release theory up to 12 hrs. And also from the table, it was also confirmed that the formulation made with 25% Ethyl cellulose showed sustained drug release. Among these, formulation F6 was optimized based on sustainity (fig-1 and 4).

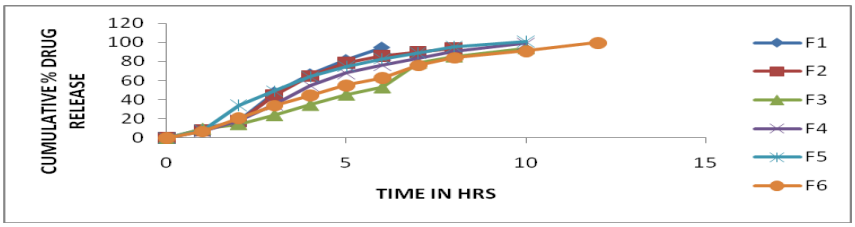

Fig-1 Dissolution graph for formulations F1-F6

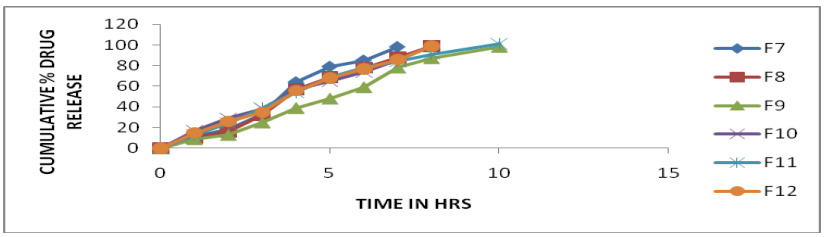

Fig-2 Dissolution graph for formulations F7-F12

CONCLUSION

Optimized formulation F6 which includes Ethyl cellulose has successfully sustained the drug release. The release process involves anomalous diffusion mechanism or diffusion coupled with erosion. FTIR studies show that there is compatability between drug and excipients for the developed matrix tablets.

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