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Formulation and Evaluation of Gastro Retentive Floating Tablets of Nimodipine

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ABSTRACT

Nimodipine is a dihydropyridine calcium channel blocker developed for the treatment of hypertension. Nimodipine has a half-life of 1.7-9 h, the bioavailability of 13% and it has restricted assimilation window in an upper part of the gastrointestinal tract (GIT), hence floating drug delivery system (FDDS) is favored. In this way, it is chosen to drag out the gastric home time as far as making drifting gastro-retentive medication conveyance framework to expand tranquilize ingestion and subsequently bioavailability. Subsequently, Nimodipine is picked as a reasonable contender for Gastric retentive medication conveyance framework, utilizing Gellan gum, Guar gum, and Tamarind gum. From the compatibility studies, it is concluded that the excipients used in the formulation were compatible with Nimodipine. Floating tablets were evaluated for pre compression and post compression parameters including floating studies, and in vitro dissolution studies.From the dissolution studies about it was reasoned that the detailing F3 containing Tamarind gum demonstrated better discharge compare to other formulations and it followed zero order kinetics with super caseII transport mechanism.

Keywords: Nimodipine, Gellan gum, Guar gum and Tamarind gum.

1. INTRODUCTION

The oral route represents the predominant and most preferable route for drug delivery unlike the majority of parenteral dosage forms it allows ease of administration by the patient and highly convenient way for substances to be introduced in to the human body. Oral drug delivery systems are divided in to immediate release and modified release systems[1]. Modified release systems have been developed to improve the pharmacokinetic profiles of active pharmaceutical ingredients and patient compliance as well as reducing side effects. Oral modified release delivery systems commonly include delayed release, extended release programmed release and site specific or timed release. Oral extended release dosage forms offer the opportunity to provide constant or nearly constant drug plasma levels over an extended period of time following administration. Extended release drug delivery systems offer several advantages compared to conventional drug delivery system including avoiding drug level fluctuations by maintenance of optimum therapeutic plasma and tissue concentrations over prolonged time periods, avoiding sub therapeutic as well as toxic concentrations, thus minimizing the risk of failure of the medical treatment and undesirable side effects, reducing the administered dose and reduced frequency of administered dose while achieving comparable results, Targeting or timing of the drug action.Hence it is highly desirable to develop sustained drug delivery system releasing the drug at predetermined rates to achieve optimal plasma drug levels and/or at the site of action[2,3].

Majority of drugs are preferentially absorbed in the upper part of the small intestine. So, Gastro retentive drug delivery systems are preferred. The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with GI mucosa leading to higher bioavailability and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus improved patient compliance[4-6].

FDDS are preferred as they are economic and has improved patient compliance and they are

advantageous for drugs absorbed from the stomach eg: ferrous salts and for drugs meant for local action in the stomach eg :antacids, drugs with narrow absorption window in the small intestine region eg: L-Dopa. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhoea, poor absorption is expected. Under such circumstances also it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response [9, 10].

The present work is an attempt to develop FDDS in the form of tablets taking Nimodipine as the model drug. Nimodipine is a calcium channel blocker used for the treatment of high blood pressure and it can also prevent vasospasm. It stabilizes voltage-gated L-type calcium channels in their inactive conformation and thus acts on vascular smooth muscle cells. By inhibiting the influx of calcium in smooth muscle cells, the drug prevents calcium dependent smooth muscle contraction and thus vasoconstriction[15,16]. It has a half-life of 8-9 h with only 13% of bioavailability and is well absorbed in the upper part of gastrointestinal tract.[17-21] Hence, floating drug delivery system is preferred such that the dosage form can release drug in a controlled manner for a longer duration. By increasing the gastric residence time bioavailability of the drug can be enhanced.

The tablets prepared by direct compression technique concentrations using direct compression technology to enhance gastric retention and to increase its bioavailability and duration of action.

2. MATERIALS AND METHODS

Materials

Nimodipine was procured from Cadila pharmaceuticals Ltd., Tamarind gum, Gellan gum and guar gum were purchased from Shreeji chemicals, Mumbai, sodium bicarbonate and other excipients were procured from B.M.R. Chemicals,Hyderabad.

Preparation of floating tablets By direct compression method:[12]

All ingredients were collected and weighed accurately. Nimodipine with polymers was filtered and gone through strainer #60 and after that, the rest of the excipients were washed over after pre-mixing all fixings in mortar for 15minutes. The whole blend was mixed for 5minutes.

At that point magnesium stearate was included and mixed again for 5-6 minutes, the lubricated powder was compressed under 8mm punch of Remake tablet punching machine, Minipress - I 12 station D tooling. The composition of different formulations is shown in the tables.

Table 1: Composition of Nimodipine floating tablets by Effervescent floating technique

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Nimodipine	30	30	30	30	30	30	30	30	30
Tamarind gum	30	60	90	-	-	-	-	--	-
Gellan Gum	-	-	-	30	60	90	-	-	-
Guar Gum	-	-	-	-	-	-	30	60	90
NAHCO3	30	30	30	30	30	30	30	30	30
MCC	133	103	73	133	103	73	133	103	73
PVP K 30	20	20	20	20	20	20	20	20	20
Mg stearate	3	3	3	3	3	3	3	3	3
Talc	4	4	4	4	4	4	4	4	4
Total wt (mg)	250	250	250	250	250	250	250	250	250

EVALUATION OF FORMULATIONS:

Pre compression parameters:

It includes Angle of repose,Bulk density,Tapped density,Cars index,Hausners ratio.

Pre compression parameters:

It includes weight variation, Hardness, Friability, Thickness and diameter, Drug content, *In-vitro* buoyancy studies, Swelling index and *In-vitro* dissolution studies.

Table 2: Precompression parameters & Post compression parameters.

Parameters	Range	Parameters	Range
Angle of repose (θ) ±SD	24.02±0.68 - 30.68±0.73	**Averagewt in (mg)±SD**	249.12±0.58-251.89±0.18
Bulkdensity (gm/cm)±SD	0.42±0.08- 0.52±0.62	**Hardness(Kg/cm2)±SD**	5.28±0.16-6.58±0.04
Tappeddensity (gm/cm) ±SD	0.48±0.01-0.60±0.03	**Thickness in (mm)±SD**	3.36±0.24-3.77±0.06
Hausnerratio (HR)±SD	1.12±0.29 - 1.18±0.35	**Friability(%)±SD**	0.19±0.86-0.74±0.56
Carr index (C.I) ±SD	11.53±0.26 - 15.51±0.22	**Drugcontent uniformity (%)±SD**	91.22±0.28-98.72±0.22

3. RESULTS AND DISCUSSION

Gastro retentive floating tablets were formulated by Nimodipine by Effervescent technique(i.e., from F1-F9) and by Non effervescent technique(i.e.,F1-F9).The formulated tablets have shown the results as given below:

UV Spectra of Nimodipine at 25µg/ml concentration. Wavelength of maximum absorption in 0.1N HCL solution was found to be 236nm**,** with uv range of 5-30µg/ml with a regression value of 0.999.

Compatibility studies by FT-IR:

From the compatibility studies it was concluded that the functional groups that were presented in the pure drug were present in the optimized formulation with very minute changes, from this we can concluded that the drug and excipients have no interactions.

***In vitro* floating buoyancy studies:**

All the formulated tablets were evaluated for the buoyancy studies for the determination of Floating Lag Time and Total Floating Time. The formulations having higher polymer concentrations exhibits total floating time for more than 12hours than the other formulations.

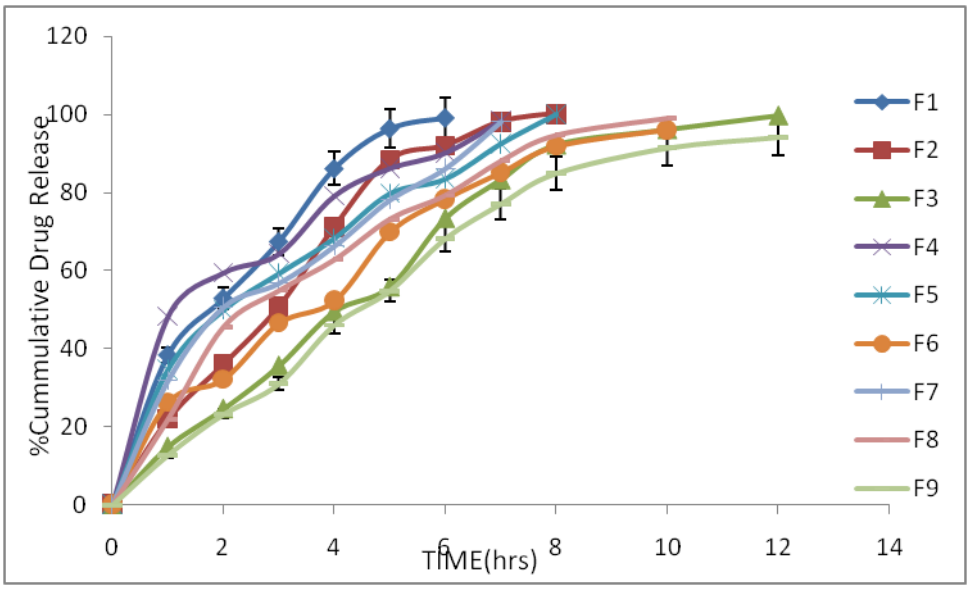

Figure 1: %CDR of F1-F9

***IN-VITRO* DRUG RELEASE STUDIES**

The In-vitro drug release data was given in tables 5.6 to 5.16 and drug release profiles are shown in fig.Formulations F1-F3 containing drug and Tamarind gum in three different ratios i.e., 12%,24%, and 36% show maximum drug release as per our objective was in an F3 formulation containing 36% of Tamarind gum at the end of 12hours.

Formulations F4-F6 containing drug and Gellan gum in three different ratios i.e., 12%,24%, and 36% show maximum drug release as per our objective was in an F6 formulation containing 36% of Gellan gum at the end of 10hours, didn't maintain sustained activity among all these trails. So Gellan gum isn't suitable for formulating floating tablets.

Formulations F7-F9 containing drug and Guar gum in three different ratios i.e., 12%,24%, and 36% show maximum drug release as per our objective was in an F6 formulation containing 36% of Guar gum at the end of 12hours, but it shows 94% of the drug release at the end of 12hours.

So by comparing all the dissolution studies of floating gastro-retentive tablets of Nimodipine, it was concluded that the 36% of tamarind gum was suitable for formulation when compared with Gellan gum and Guar gum. So the drug release kinetics were performed for the F3 formulation containing 36% of tamarind gum.

4. CONCLUSION

Gastro retentive floating tablets of Nimodipine were formulated using tamarind gum, Gillan gum and Guar gum in three different ratios. From the compatibility studies, it is concluded that the excipients used in the formulation were compatible with drug Nimodipine and thus suitable for the formulation of Nimodipine floating tablets. Nimodipine tablets were fabricated by direct compression method. In-vitro buoyancy studies were performed for all the formulations, F1 to F9 by using 0.1 N HCl solution at 370C. Tablet containing Tamarind gum (F3) showed good buoyancy with very short lag time and long floatation time of more than 12 hrs in 0.1 N HCl. In-Vitro release study is performed for 12 hrs. An optimized formula containing Tamarind gum (F3) showed better release compare to other formulations and it followed zero order kinetics with the super case transport mechanism. From this study, it was concluded that Tamarind gum can be used in the formulation of Nimodipine sustained release gastro-retentive floating drug delivery system. Overall, this study concludes that viscosity of the polymer is a major factor affecting the drug release and floating properties of GRDDS.

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