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NATURAL AND SYNTHETIC POLYMER BASED MOUTH DISSOLVING TABLET OF CLOPIDOGREL

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ABSTRACT

Difficulties of swallowing and first-pass metabolism are of the major limitations of oral medicaments resulting in patient non-compliance and poor oral bioavailability. Many of the drawbacks in that can be avoided by the administration of another dosage forms e.g. Mouth Dissolving Tablets (MDTs) that dissolve upon contact with saliva and consequently allowing systemic drug absorption via buccal mucosa. This study aimed to prepare MDTs prepared by Clopidogrel containing disintegrants. MDTs were prepared using different other excipients where powdered blends were evaluated to investigate their flow properties followed by physical evaluation of the directly compressed tablets.

KEYWORDS

Mouth dissolving tablets (MDTS), Clopidogrel, Disintegrants and Compressed tablets.

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INTRODUCTION

Quick dissolving tablets are characterized as "A strong measurement structure containing restorative substances, which breaks down quickly, as a rule inside only seconds, when put upon the tongue" in the event of regular tablets, actual issues with gulping (dysphagia) can happen at whatever stage in life however are especially predominant in the old and those with dementia, though refusal to swallow is frequently experienced in geriatric, pediatric and mental patients. Troubles and protection from tablet-taking are basic in all understanding gatherings. Lately, quick dissolving tablets have been created to defeat issues identified with gulping troubles. Quick Dissolve, Quick

Dissolve, Rapid Melt, Quick Disintegrating, Mouth Dissolving, Orally Disintegrating, Oro Dispersible, Melt-in-Mouth, and so on are terms that address a similar medication conveyance frameworks. The orally crumbling property of tablet is ascribed to a fast entrance of water into the tablet framework, which makes permeable design and result in quick deterioration. At the point when put on tongue, these tablets crumbles promptly, delivering the medication which breaks down or scatters in spit. The medications might be consumed from mouth, pharynx or throat as the salivation passes down into the stomach. Benefits of the Fast dissolving tablets incorporate simplicity of gulping without the guide of water, quick beginning of activity, upgraded disintegration rate, expanded gastric retention, improved oral bioavailability, limited first pass digestion and improved patient consistence[1-3].

The primary goal of the current exploration work is to form the Clopidogrel Fast Dissolving tablets. Clopidogrel, an antiplatelet drug, has a place with BCS Class-II and used to control Heart assault, Hypertension by restraining Platelet enactment and accumulation. The Fast Dissolving tablets of Clopidogrel were readied utilizing Potato starch and Sodium starch glycolate as a Superdisintegrant by Direct Compression procedure utilizing 3^2 factorial plan[4-7].

MATERIAL AND METHODS

Materials

Clopidogrel were received as gift sample from Cipla Pharmaceutics, Satara. Potato starch, Sodium Starch Glycolate, Microcrystalline cellulose and Avicel PH 102 were procured from SD Lab chem. Centre Mumbai. All other chemicals used were of analytical reagent grade.

Method

Fast dissolving tablets of Clopidogrel were prepared by direct compression Method as per formulae given in Table. The super disintegrants (sodium starch glycolate, potato starch) in varying concentration. All the ingredients were passed through # 60. All the ingredients were mixed in a motor and pestle for 5 min. The mixed blend was compressed into tablets on a Lab press tablet compression machine to a weight of 500mg each, with thickness of 4.2±0.15mm and diameter of 13mm. The prepared tablets were evaluated for the uniformity of weight, drug content, hardness, friability, dispersion time and disintegration time. In solid dosage forms the physiochemical properties of blend rules the tablet quality. The mixing step if not properly optimized can affect the characteristics of blend and thereby tablet produced. The blends were characterized by mass-volume relationship (bulk density, tapped density, Hausner's ratio, compressibility index) and flow properties)[8].

MILLING → SEIVING → MIXING → COMPRESSION

Evaluation Parameters

Pre-compression studies of fast disintegrant tablet granules

Fourier Transform Infrared Spectroscopy[9]

The Fourier change infra-red investigation was directed for the construction portrayal. FTIR spectra of the unadulterated medication Clopidogrel. Around 5mg of tests were blended in with 50mg of spectroscopic evaluation KBr, tests were checked in the IR range from 500 to 3500cm-1, with a goal of 4cm-1.

Pre-pressure investigations of quick disintegrant tablet granules.

Mass density[10]

It is proportion of absolute mass of powder to the mass volume of powder. It was estimated by emptying the gauged powder into an estimating chamber and volume was noted as mass thickness (Db)

It communicated in gm/cc and is given by: Db =M/Vb

Where, M= is the mass of powder.

Vb= is the mass volume of powder.

Tapped Density[10]

It is the proportion of all out mass of powdered to the tapped volume of powder. The tapped volume was estimated by tapping the powder to a steady volume.

It is communicated in gm/cc and is given by: Dt =M/Dt

Where, M= is the mass of powder.
Vt = is the tapped volume of the powder.

Hauser Ratio[11]

Hausner Ratio is an aberrant file of simplicity of powder stream. It is determined by the accompanying equation:
Hausner Ratio =Dt/Db
Where, Dt = Tapped thickness
Db = Bulk thickness
Hausner Ratio worth of powder show in table

Growing index[12]

The examination was done utilizing a 100ml stoppered graduated chamber. The underlying mass volume of 1gm of starch was noted water was included adequate amount of water to deliver 100ml of a uniform scattering and was put away at room temperature and the dregs volume of the swollen mass was estimated following 24 hour.

Carr's file (I)[13]

It shows the straightforwardness with which a material can be instigated to stream. It is communicated as a rate and is given by
Carr's list (%) = (Tapped thickness – Pour thickness)/Tapped densityX100
Carr's list upsides of powder show in table

Point of rest (θ)[13]

The frictional power in a free powder can be estimated by the point of rest. It is characterized as most extreme point conceivable between the openly sliding surface of a heap of powder and the flat plane.
Tan θ =tan-1(h/r)
Where, θ = is the point of rest
h=is the tallness
r =is the range
Stream properties and relating point of rest.

Post-compression studies Clopidogrel fast disintegrant tablets

Hardness or Crushing strength Test[13]

Hardness of the tablet was resolved utilizing the Monsanto hardness analyzer (The lower unclogger was set in contact with the tablet and a zero perusing was taken. The unclogged was then constrained against a spring by tuning a strung bolt until the tablet cracked. As the spring was packed a pointer rides along a measure in the barrel to demonstrate the power. The power needed to break the tablet is estimated in kilograms and a devastating strength of 4Kg is typically viewed as the base for agreeable tablets. Oral tablets typically have a hardness of 4 to 10 kg; be that as it may, hypodermic and chewable tablets have a hardness of 3kg and some supported delivery tablets have a hardness of 10-20 kg5.

Thickness Test[14]

The thickness of the tablet is for the most part identified with the tablet hardness can be utilizes as beginning control boundary. Ten tablets were arbitrarily chosen from every tablet thickness was resolved utilizing a Vernier caliper and the perusing was recorded in millimeters.

Friability Test[15]

The pre-gauged tablets were put in the friabilator (EF-2, Electro lab, Mumbai) which was then worked for 100rpm, at that point tidied and rechecked. The Conventional packed tablets that lose under 0.5-1.0% of their weight are for the most part thought to be adequate.
Friability record = I-F/IX 100
Where,
I - Initial weight, F - Final weight
Weight variety test 24
Loads of 20 individual tablets were noted and their mean weight likewise determined. The rate deviation was determined by utilizing the accompanying recipe,
Rate deviation = [X-X*/X] × 100
X - Actual load of the tablet,
X*-Average load of the tablet

Assessment of Drug Content[16]

A precisely gauged measure of powdered Clopidogrel (100mg) was separated with water and the arrangement was sifted through 0.45µ film channel paper. The absorbance was estimated at 275 nm after appropriate dilution 6.
Estimation
The measure of Clopidogrel present in tablet can be determined utilizing the recipe
At/As x Sw/100 x 100
Where,

At = Absorbance of test planning,
As = Absorbance of Standard planning,
Sw = weight at Clopidogrel working norm (mg)

***In vitro* Drug Release Studies**[17-19]

The in vitro drug discharge study was done for 24 hours utilizing USP paddle type disintegration test device in phosphate cushion (pH 6.8) at 75 rpm keeping up temperature at 37±0.50c. A 10ml of tests were gathered from every vessel at 0, 2, 4, 8, 12, 16 and 24 hours and investigated by UV spectrophotometer at 275nm. The removed example was promptly supplanted by equivalent volume of new cradle. The disintegration information got were plotted as rate drug discharge versus time

***In Vitro* Disintegration**[20-23]

Six tablets of every plan were utilized to decide crumbling time. Phosphate cushion (pH 6.8) was utilized as a breaking down medium and temperature was looked after 37±0.50C. Normal breaking down season of six tablets was resolved. Phosphate cradle Media volume 900ml.

RESULTS AND DISCUSSION

Table No.1: Formulation of mouth dissolving tablet prepared by Direct Compression method

S.No	INGREDIENT	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	Clopidogrel	75	75	75	75	75	75	75	75	75	75
2	Sodium starch glycolate	50	50	50	50	50	-	-	-	-	-
3	Potato starch	-	-	-	-	-	50	50	50	50	50
4	Magnesium stearate	25	25	25	25	25	25	25	25	25	25
5	Microcrystalline cellulose	100	100	100	100	100	100	100	100	100	100
6	Avicel ph 102	225	225	225	225	225	225	225	225	225	225
7	Talc	25	25	25	25	25	25	25	25	25	25
8	TOTAL	500	500	500	500	500	500	500	500	500	500

Table No.2: Pre-compression studies of fast disintegrant tablet granules

Formulation	A Angle of repose	Bulk density	Tapped density	Carr's index	Haushner's ratio
F1	28.10	0.25	0.25	0	1
F2	29.29	0.24	O.25	4	1.04
F3	29.59	O.25	0.26	3	1.04
F4	29.59	0.25	0.26	3.8	1.04
F5	27.74	0.26	0.27	3.7	1.03
F6	28.23	0.25	0.25	0	1
F7	28.89	0.23	0.25	8	1.08
F8	29.59	0.23	0.23	0	1
F9	29.59	O.25	0.26	3	1.04
F10	27.74	0.26	0.27	3.7	1.03

Table No.3: Evaluation of prepared Clopidogrel MDT

Formulation code	Hardness (Kg/cm2)	Uniformity of weight (mg)	Friability (%)	Wetting Time(sec)	Disintegration Time(sec)
F1	3.1	501	0.309	26	22
F2	3.2	502	0.402	25	20
F3	3.4	501	0.309	24	17
F4	3.1	500	0.400	23	17
F5	3.2	499	0.418	24	19
F6	3.1	501	0.309	26	18
F7	4	502	0.399	24	17
F8	3.5	498	0.401	22	16

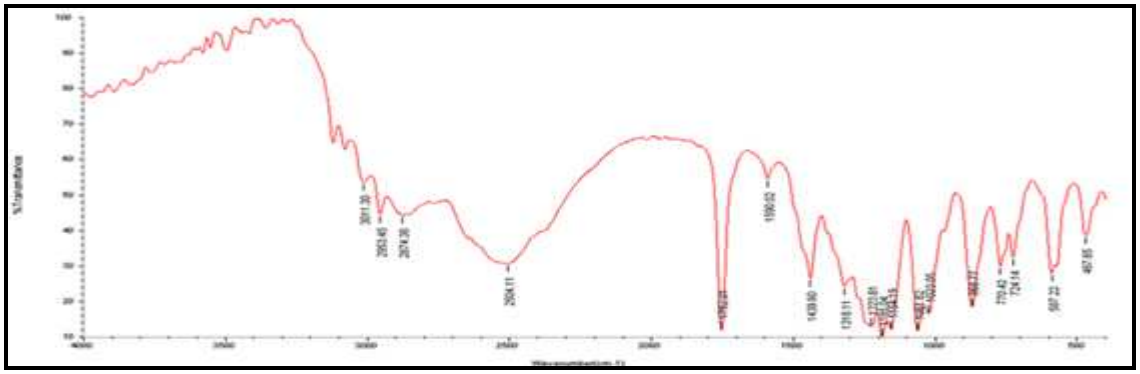

Figure No.1: IR Spectra of Clopidogrel

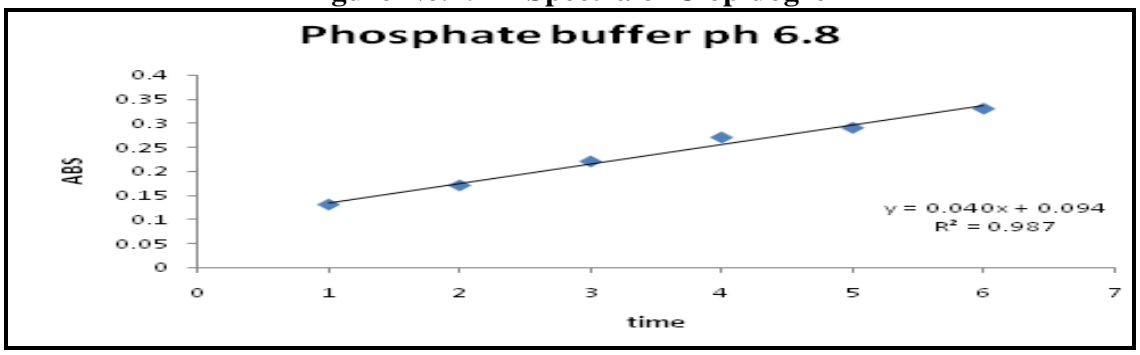

Figure No.2: Dissolution studies of Clopidogrel MDT using Potato starch as superdisintegrant

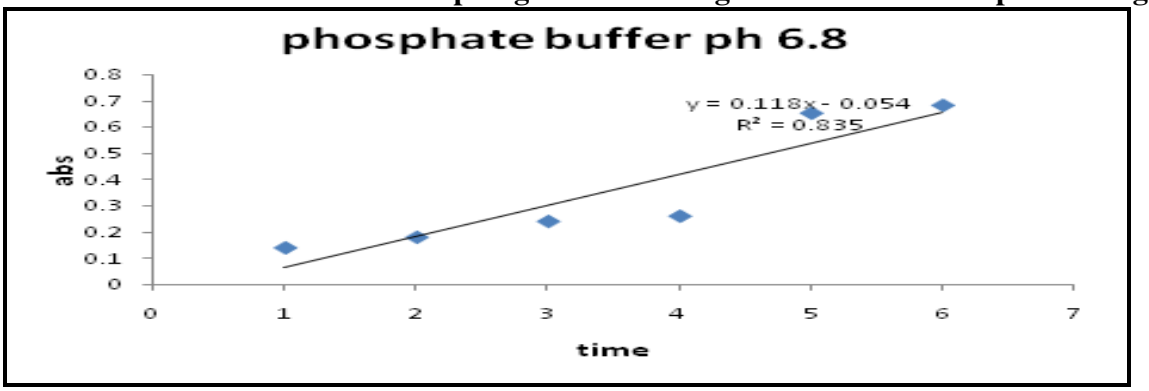

Figure No.3: Dissolution studies of Clopidogrel MDT using sodium starch glycolate a superdisintegrant

CONCLUSION

Preformulation studies of Clopidogrel were performed, the FT-IR analysis revealed that the superdisintegrants and excipients used were compatible with Clopidogrel. Fast dissolving tablets Ciprofloxacin can be prepared by direct compression technique using superdisintegrants, namely potato starch and sodium starch glycolate. Amongst all the formulations, formulation containing sodium starch glycolate as super disintegrant is fulfilling all the parameters satisfactorily. It has shown excellent in vitro disintegration, in vitro dispersion time compared to potato starch.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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