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Original Article

Formulation and *in-vitro* dissolution of Clopidogrel tablet by using sodium starch glycolate and natural xanthan gum

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ABSTRACT

Different formulations were made with an aim to develop stable, cost effective Clopidogrel tablets by direct compression technique. Four formulations (F1 – F4) having Primojel and xanthan gum at different concentrations level were prepared. The prepared batches of tablets were evaluated for hardness, friability, disintegration and *in-vitro* dissolution study. All The formulations containing combination of Primojel and Xanthan gum showed different *in-vitro* disintegration time and drug release.

1. INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug in the proper site in the body to achieve promptly and then to maintain the desired drug concentration [1-3]. That is, the drug delivery system should deliver drug at a rate dedicated by the needs of the body over a specified period of treatment. Tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness and ease in manufacturing [4]. They can be mass produced with robust quality controls and other different branding possibilities by means of colored film coating different sizes and shapes for better appearance and improving the patient compliance [5-8]. Clopidogrel is an inhibitor of platelet aggregation used in the management and prevention of thromboembolic disorders. It is used as adenosine diphosphate receptor antagonists in an anti platelet therapy. It is efficacy in reducing the stroke is similar or more to that of aspirin. Pharmaceutical excipients can be defined as any substance other than the active and is included in the formulation for improving the pharmacokinetic parameters. Corn Starch, Primojel, are some of the super-disintegrants included in the immediate release tablets for better onset of action [9-14].

2. EXPERIMENTAL

2.1 Chemicals

Clopidogrel bisulphate, Xanthan gum, Corn Starch, Primojel, Talc, Ethyl cellulose, Lactose were obtained from the college. All the materials were of pharmacopoeia grade.

2.2 Procedure

Tablets were prepared by direct compression method and various formula used in the formulation are shown in table. Each formulation having different ratios of following ingredients are mixed uniformly.

Table 1: Formulation of film coated Clopidogrel tablets

Ingredients (mg)	**Formulation** (F1)	**Formulation** (F2)	**Formulation** (F3)	**Formulation** (F4)
Clopidogrel	75	75	75	75
Xanthan gum	25	50	75	92
Corn Starch	60	60	60	60
Primojel	67	42	17	00
Talk	4	4	4	4
Ethyl cellulose	64	64	64	64
Lactose	40	40	40	40
	335 mg	**335 mg**	**335 mg**	**335 mg**

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2.3 Preparation of coating solution

3000 mg of accurately weighed corn-starch was added in 100 mL of distilled water to obtained 3 % w/v of solution and stirring was carried out using a propeller stirrer (Remi, Mumbai, India) at 1000 rpm for 45 min.

2.4 Coating of tablets

The tablets were film-coated using a side-vented, perforated pan coating machine (Neo Machine Mfg. Co. Pvt. Ltd. Calcutta, India). Inlet air spray-rate and exhaust air spray-rate were kept constant at 150 f3 / m and 200 f3 / m, respectively. First fixed quantity (2 kg) tablets were kept in the pan which was pre-adjusted at 50° C temperature for 10 min. Then actual weight of tablet was determined. Then, various parameters like spray rate, inlet air temperature and rotating speed of pan were adjusted and studied with different levels. After finishing of the coating tablets were kept in the pan at 60° C and 2 rpm for curing. Then tablets were removed from the pan and evaluated.

Table 2: Coating formula for film coated Clopidogrel tablets

Sl. No.	Ingredients	Uses	Qty./1000 Tablet (gm)
1.	Hypromellose	Film forming agent	6.60
2.	Lactose monohydrate	Filler	0.69
3.	Titanium dioxide	Opacifier	3.72
4.	Triacetin	Plasticizer	1.38
5.	Iron oxide red	Color	0.03
6.	Purified water	Vehicle	95.00

2.5 Characterization of drug

Identification of drug: The drug was identified by, Ultraviolet spectroscopy (UV) and melting point.

(I) Ultraviolet Spectroscopy: A stock solution of Clopidogrel (100 mcg/ml) in phosphate buffer of pH 7.2 was prepared. And scanned spectrophotometrically between 200-400 nm.

(II) Melting point: The melting point of Clopidogrel sample was determined by melting point apparatus and found to be 158 °C.

(III) Preparation of buffer solution of pH 7.2: Weight separately both Potassium dihydrogen orthophosphate (KH_2PO_4) & Sodium Hydroxide (NaOH) to their respective amount (given below) for 1l tr distilled water and mixed them thoroughly.

KH_2PO4 - 6.805 gm

NaOH - 1.388 gm

2.6 Preparation of calibration curve

A stock solution of Clopidogrel (100mcg/ml) in phosphate buffer of pH 7.2 was prepared. A series of dilutions containing 2, 4, 6, 8, and 10 mg/ml of Clopidogrel were prepared and the absorbance was measured at 219 nm spectrophotometrically. A linear regression was drawn by plotting absorbance against concentration (Figure No. 1), the regression coefficient was also determined.

Table 3: Calibration curve of Clopidogrel

Concentration (µg/ml)	Absorbance
2	0.091
4	0.198
6	0.315
8	0.412
10	0.528

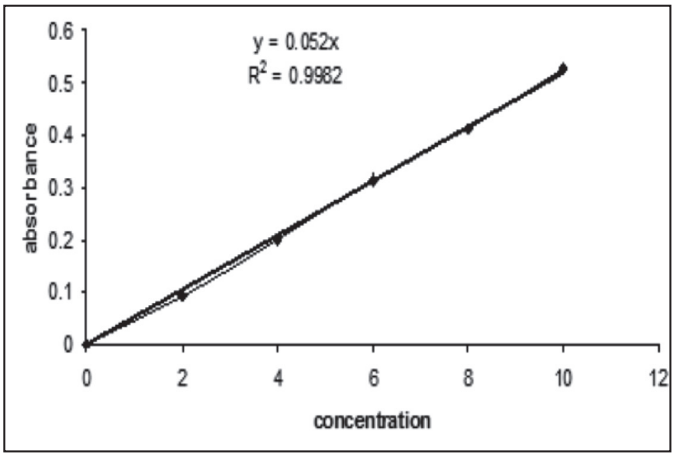

Fig. 1. Calibration curve of Clopidogrel

2.7 *In-vitro* drug release study

The in-vitro release of Clopidogrel film coated tablet was monitored in phosphate buffer, pH 7.2 at 37º C ± 1º C using USP basket type dissolution rate test apparatus. The tablet of different formulations (wt. equivalent to 75 mg pure drug) was stirred in 900 ml dissolution medium at 75 rpm. Samples (10 ml) were withdrawn at predetermined time interval and replenished immediately with the same volume of fresh medium. Aliquot's following suitable dilution, were analyzed spectrophotometrically at 219 nm. The concentrations of Clopidogrel in test samples were corrected for sampling effect. The drug release experiments were conducted in triplicates. Following the above manner, the dissolution of pure drug was also carried out [15-16].

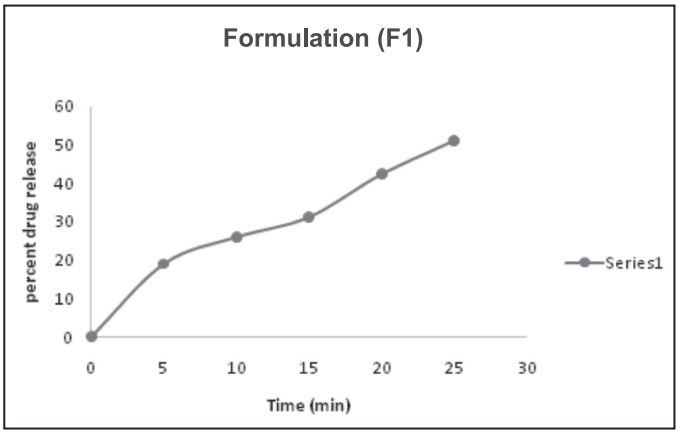

Fig. 2. *In- vitro* Dissolution Study of Clopidogrel F_1

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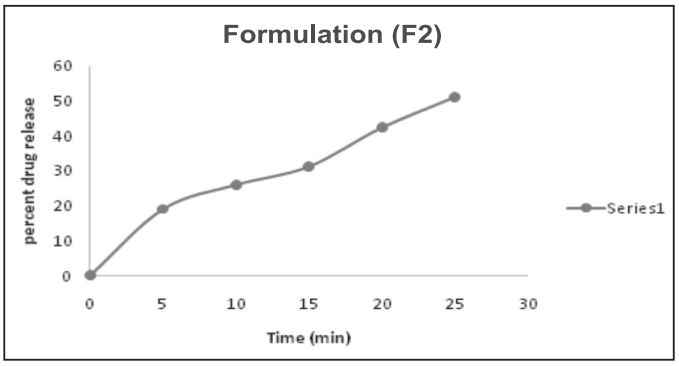

Fig. 3. *In -vitro* dissolution study of Clopidogrel F_2

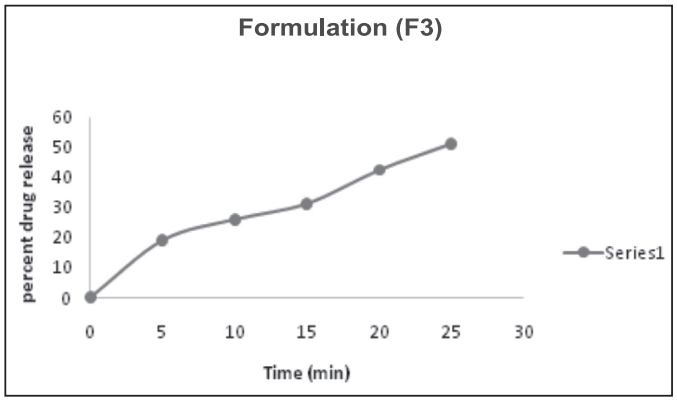

Fig. 4. *In vitro* Dissolution Study of Clopidogrel F_3

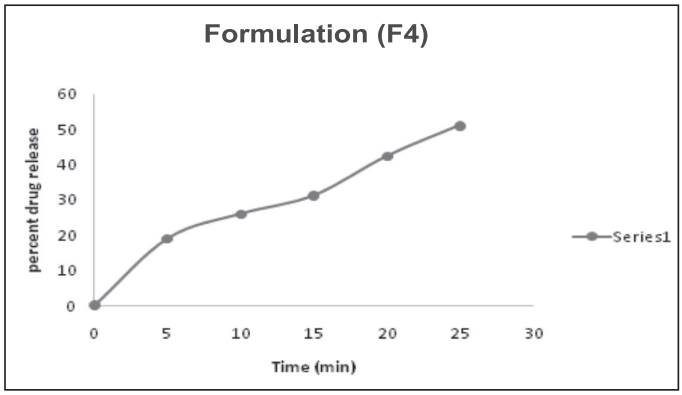

Fig. 5. *In vitro* Dissolution Study of Clopidogrel F_4

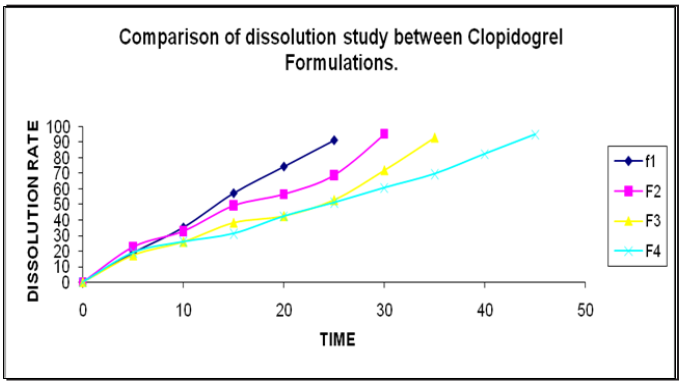

Fig. 6. Comparison of dissolution study between Clopidogrel Formulations

3. RESULTS AND DISCUSSION

All four batches were prepared under same conditions and on same instruments to minimize variations. Super disintegrants are generally used by formulation scientist for developing FDTs or for improvement of solubility of drugs. The primary requirements of all four formulations are quicker disintegration time. The dissolution rate of Clopidogrel FDTs of different batches are shown [figure 6]. The weight variation of 155 mg tablets was found maximum up to ± 1.2 % RSD. Hardness was found to be within 3.5 to 4.0 kg/cm^2 which limit friability within 0.4 % only. The drug Contents was found to be within limits and all tablets were passing the dispersion test.

4. CONCLUSION

The evaluation results of all four batches were found to be satisfactory within limit and the disintegration time of Primojel was quite good with presence of xanthan gum. This clearly indicates that Primojel has good disintegrating property on addition of sodium starch glycolate with xanthan gum. In present study super disintegrant like sodium starch glycolate shows less disintegration time and as the concentration of xanthan gum increases dissolution time also increases. Hence it proofs success of natural xanthan gum in orally disintegrating tablets formulation at very low concentration and cost.

REFERENCES

[1] Jayesh, P.; Manish, R. Tablet formulation design and manufacture: Oral immediate release application. *Pharma Times* **2009**, 41(4), 21-29.

[2] E. Braunwald, D.; Angiolillo, E.; Bates, P.; Berger, D.; Bhatt, C.; Cannon, M.; Furman, P.; Gurbel, A.; Michelson, E.; Peterson, S.; *Wiviott* **2008**, 31(S1),I2.

[3] Iida, O.; Nanto, S.; Uematsu, M.; Morozumi, T.; Kitakaze, M.; Nagata, S. Cilostazol reduces restenosis after endovascular therapy in patients with femoropopliteal lesions. *J Vasc Surg* **2008,** 31, 48(1), 144-9.

[4] Satoskar, R.S.; Bhandarkar, S.D.; Nirmala,N.R. *Pharmacology and Pharmacotherapeutics* **2005**; 19th ed., 471.

[5] Rang, H.P.; Dale, M.M.; Ritter, J.M.; Flower, R.J. Pharmacology **2007**; 6th ed: 342.

[6] Ram, V.; Kher, G.; Dubal, K.; Dodiya, B.; Joshi, H. Development and validation of a stability indicating UPLC method for determination of ticlopidine hydrochloride in its tablet formulation. *Saudi Pharma J* **2011**, 31,19(3),159-64.

[7] Badorc, A.; Frehel, D.; inventors; Sanofi, assignee. Dextro-rotatory enantiomer of methyl alpha-5 (4, 5, 6, 7-tetrahydro (3, 2-c) thieno pyridyl) (2-chlorophenyl)-acetate and the pharmaceutical compositions containing it. *United States patent US* **1989**, 4,847,265.

[8] Fiese, E.F.; Hagen, T.A. Preformulation. In: Lachman L, Lieber man, H.A, Kanig, J.L. The theory and practice of industrial pharmacy. Mumbai, Varghese Publishing House, 3rd ed., **1987**, 182-184.

[9] Ansel, H.C.; Popovich, N.G.; Allen, L.V. Pharmaceutical dosage forms and drug delivery system. 8th ed. New Delhi. B.I. Waverly Pvt. Ltd., **1995**, 189-194 & 235-236.

[9] Lachman, L.; Liberman, H.A.; Kanig, J. The theory and practice of industrial pharmacy, Varghese publishing house, 3rd ed., New York, **1989**, 293-373.

[10] Chowdhury, S.; Majumdar, S. Statistical optimization of fixed dose combination of glimepiride and atorvastatin calcium in immediate release tablet formulation. *Int J Pharm Sci* **2010**, 10, 2(4), 194-200.

[11] Savi, P.; Zachayus, J.L.; Delesque-Touchard, N.; Labouret, C.; Hervé, C.; Uzabiaga, M.F.; Pereillo, J.M.; Culouscou, J.M.; Bono, F.; Ferrara, P.; Herbert, J.M. The active metabolite of Clopidogrel disrupts P2Y12 receptor oligomers and partitions them out of lipid rafts. Proceedings of the *National Academy of Sciences (NAS)* **2006**, 103 (29), 11069-74.

[12] Zakaria, A.; Bandarenko, N.; Pandey, D.K. Clopidogrel-Associated TTP: An Update of Pharmacovigilance Efforts Conducted by Independent Researchers, Pharmaceutical Suppliers, and the Food and Drug Administration". *Stroke* **2004**, 35, (2), 533–8.

[13] Diener, H.C.; Bogousslavsky, J.; Brass, L.M. "Aspirin and Clopidogrel compared with Clopidogrel alone after recent ischemic stroke or transient ischemic attack in high-risk patients (MATCH): randomized, double-blind, placebo-controlled trial". The Lancet, **2004**, 364 (9431): 331–7. 16.

[14] Topol, E. The creative destruction of medicine: How the digital revolution will create better health care. Basic Books, **2013**, 13.

[15] Food and Drug Administration. Public-health advisory: updated safety information about a drug interaction between clopidogrel bisulfate (marketed as Plavix) and omeprazole (marketed as Prilosec and Prilosec OTC). Public Health Advisories/ucm190825.