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Formulation and Evaluation of Enteric coated tablets of Mycophenolate Sodium

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ABSTRACT

This study briefly describes the Formulation and evaluation of Enteric coated tablets of Mycophenolate sodium, Containing Mycophenolate sodium as API belongs to category antiproliferative Inhibitors which inhibits Inosine Monophosphate dehydrogenase.The Entering Coating was done by using 2 polymers (cellulose acetate phthalate and Eudragit L). The Conclusion is that the Enteric coating tablet of Mycophenolate sodium which was formed by Dip coating method containing cellulose acetate phthalate as enteric coating solution in concentration of 0.21±0.07% will provide drug Content in 98.04 % and that of Eudragit L in the concentration of 0.24±0.08 will provide drug content in 97%.

Key World: Enteric coating, Mycophenolate sodium, Antiproliferative inhibitors, Cellulose acetate phthalate, Eudragit L.

INTRODUCTION

Tablet Coating: The Tablet Coating is very simple. we coat the tablet with the polymer solution to delay the drug release.

- The principles of tablet Coating includes the following: To mask the taste, odor, or color of the drug[1].
- To Improvise physical and chemical protection of the drug
- To control the release of the drug from the tablet and release the drug at desired place[2].
- To protect the drug from the gastric environment of the stomach with an acid-resistant enteric coating[3].
- To incorporate another drug or formula adjuvant in the coating to avoid chemical incompatibilities or to provide sequential drug release[4].

The Properties of Tablets and that of the Coating Solution are equally important.

Various types of Polymers Used in preparation of Coating Solution.
Cellulose Acetate Pthalate: Cellulose Acetate Phthalate is soluble above PH 6.
It is also hygroscopic and relatively permeable to moisture and gastric fluids, in comparison with some other enteric polymers[5].
CAP films are best suited with hydrophobic materials to form brittle enteric coating film.

The Acrylate Polymers: this Polymers are also soluble at intestinal PH 6 to 7.
They also best suited for the Enteric Coating film.
Two commercial forms are available: EUDRAGIT-L and EUDRAGIT-S.
Eudragit L is available as an organic solution (Isopropanol), solid, or aqueous dispersion. Eudragit S is available only as an organic solution (Isopropanol) and solid[6].

DIP Coating method:
Dip coating is a widely utilized technique in various industries for manufacturing purposes[7].

advantage of dip coating, when compared to other processing techniques, is its Simple design. It is a cost-effective solution that requires minimal setup and maintenance. Additionally, it has the capability to generate films with an exceptional level of uniformity and nanometer-scale roughness[8].

The Four areas which are important in DIP coating are:[9,10,11,12]

- The principles of tablet Coating includes the following: To mask the taste, odor, or color of the drug.
- The static meniscus, in which the hydrostatic equilibrium determines the meniscus's shape.
- The area surrounding the stagnation point is known as the dynamic meniscus. The equilibrium between the entraining and draining forces is known as the stagnation point.
- Where the wet film has attained a specific thickness (h^0), known as the constant thickness zone.
- The area where the wet film starts, known as the wetting zone

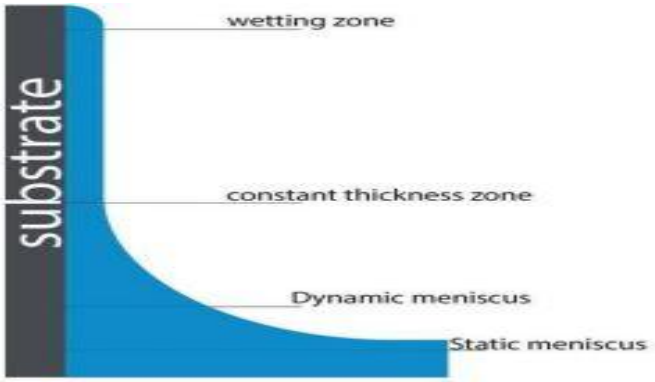

Fig.no.1 The dip coating formation involves four distinct region. These are the static meniscus, the dynamic meniscus, the constant thickness zone, and the wetting zone[13].

MATERIALS AND METHODS

Mycophenolate sodium was received from Signet Chemical Corporation. Microcrystalline cellulose was received from Cipla Pharma, Mumbai, India. Povidone K30 was received from SD Pharma, Mumbai, India[14]. Mannitol received from Signet Chemical Corporation dicalcium Phosphate received from Fine Chem Industries, India talc received from Spectrochem Pvt. Ltd. Mumbai. magnesium stearate received from Spectrochem Pvt. Ltd. Mumbai[15].

PROCEDURE:

1. Preparation of Mycophenolate sodium tablets:

a. Preparation of powder blend[16]

Mycophenolate sodium powder blend for tableting were prepared by direct compression method. Specified quantity of Mycophenolate, croscarmellose sodium, mannitol, calcium phosphate, and MCC were weighed according to thes formula (**Table 3**) and transferred in a mortar and pestle and mixed thoroughly. The powder was passed through sieve no 80 to obtain the granules. The specifiedquantity of magnesium stearate and talc were finally added and mixed for the compression of tablets.

2. Preparation of Mycophenolate sodium tablets[17,18,19]

An ideal mixture of granules was directly punched into tablets weighing about 200 mg containing 40 mg of Mycophenolate sodium, using rotary tablet compression machine (Riddhi 10 stn mini tablet press RDB4-10, Rimek, Ahmedabad, India), using 8 mm diameter concave punches. The different batches of Mycophenolate tablets were collected and stored in air tight containers.

Table No.1 Composition of Mycophenolate sodium enteric coated sodium tablets:

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Mycophenolate sodium	180	180	180	180	180	180	180	180	180
Microcystaline cellulose	18	18	18	36	36	36	54	54	54
Povidone K30	7.2	12.6	18	7.2	12.6	18	7.2	12.6	18
Dicalcium Phosphate	50	50	50	50	50	50	50	50	50
Talc	14	14	14	14	14	14	14	14	14
Magnesium stearate	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6
Mannitol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Bulk Density :
The apparent true density (ρb) was measured by pouring the pre weighed (M) blend into a graduated cylinder. The bulk volume (Vb) of the blend was determined by this method. Then the true density was determined by the given below formula.
ρb = M/Vb

Tap Density:
The measured cylinder containing a known mass (M) of blend was tapped for a fixed time, and the minimum volume (Vt) occupied in the cylinder was measured. The tapped density was calculated by the formula mentioned below.
Tap density = M/Vt

Carr's Index:
Based on the apparent bulk density and the tapped density, the percentage compressibility of the bulk drug was determined by using the following formula.
% Compressibility = (tapped density - bulk density/tapped density) X100

Hausner's Ratio :
The ratio of tapped density to bulk density of the powders is called the Hausner's ratio.

Angle of Repose:
The angle of repose was determined by the funnel method. The determination of angle of repose by this method is referred to as static angle of repose. Powder is poured onto the center of the dish from the funnel that can be raised vertically until the maximum cone height (h) is obtained. The angle of repose can be calculated by the given formula,
α = tan-1(h/r)
Where h is height of pile and r is radius of pile.

RESULT AND DISCUSSION

Preformulation parameters:
Table No. 02 Pre compression parameters of Mycophenolate Sodium Enteric Coated Tablets:
Precompression parameters include Bulk Density, Tapped density, Carr's Index, Hausner's ratio, Angle of repose.

nulationCode	Parameter				
	Bulk density (gm/mL) *	Tapped density (gm/mL) *	Carr's Index(%)*	Hausner'sratio*	Angle of repose (Θ)*
F1	0.357±0.03	0.384±0.05	7.03±0.09	1.075±0.04	28.31±0.26
F2	0.312±0.04	0.335±0.02	6.86±0.15	1.073±0.05	27.20±0.14
F3	0.306±0.03	0.326±0.03	6.13±0.12	1.065±0.02	29.13±0.34
F4	0.312±0.03	0.334±0.06	6.58±0.14	1.070±0.06	26.13±0.26
F5	0.306±0.03	0.334±0.05	8.38±0.17	1.091±0.08	26.78±0.18
F6	0.384±0.04	0.429±0.05	10.48±0.20	1.117±0.07	25.79±0.24
F7	0.358±0.05	0.385±0.04	7.01±0.13	1.075±0.03	29.52±0.14
F8	0.286±0.05	0.313±0.04	8.62±0.07	1.094±0.03	26.95 ±0.15
F9	0.348±0.08	0.328±0.05	5.74±0.13	1.06±0.08	26.13±0.26

*****Mean ± SD n=3

Table No.03 Post compression parameters of Mycophenolate sodium core tablets

FormulationCode	Parameter				
	Hardness 2(Kg/cm)*	Friability(%)*	Weight variation(mg) *	Drug content(%)*	Disintegration time(min) *
F1	5.80 ± 0.12	0.69 ± 0.015	199 ± 0.12	96.28 ± 0.15	10.6± 0.62
F2	5.56 ± 0.24	0.51 ± 0.017	206 ± 0.24	97.62 ± 0.27	8.26± 0.56
F3	5.83 ± 0.08	0.48 ± 0.014	201 ± 0.17	99.51 ± 0.36	5.38± 0.23
F4	4.93 ± 0.15	0.64 ± 0.015	208 ± 0.20	98.17 ± 0.16	11.48± 0.15
F5	5.73 ± 0.25	0.71 ± 0.016	203 ± 0.16	98.92 ± 0.42	9.32± 0.18

F6	5.12 ± 0.34	0.68 ± 0.026	206 ± 0.14	100.34 ± 0.13	6.13± 0.25
F7	5.66 ± 0.17	0.54 ± 0.026	199 ± 0.22	98.50 ± 0.48	10.54± 0.43
F8	6.20 ± 0.35	0.49 ± 0.025	204 ± 0.18	98.41 ± 0.34	9.12± 0.71
F9	5.60 ± 0.24	0.42 ± 0.018	198 ± 0.15	99.08 ± 0.35	6.02± 0.21

* Mean ± SD, n=3

Two batches F3 and F9 shows the satisfactorily results in Disintegration test. Therefore they have been selected for the further research which accompanies the Enteric polymer coating of cellulose acetate Phthalate and Eudragit L. The cellulose acetate phthalate is used in highest concentration.

Table No.04 Physicochemical evaluation parameters of enteric coated tablets

Polymer	**Batch Code**	**Parameter**		
		Weight Variation (mg) *	**HardnessKg/cm^2***	**; content(%)***
CAP	C1F3	211 ± 0.035	6.5 ± 0.15	96.75 ± 0.14
	C2F3	214 ± 0.016	5.9 ± 0.24	93.65 ± 0.35
	C1F9	212 ± 0.006	5.4 ± 0.09	94.45 ± 0.26
	C2F9	210 ± 0.024	6.3 ± 0.14	98.54 ± 0.12
Eudragit L 100	E1F3	214 ± 0.021	5.5 ± 0.16	93.47 ± 0.23
	E2F3	213 ± 0.012	6.0 ± 0.06	94.56 ± 0.14
	E1F9	215 ± 0.015	6.5 ± 0.31	98.27 ± 0.45
	E2F9	211 ± 0.024	5.7 ± 0.20	96.35 ± 0.12

Table No.05. *In vitro* drug release of Mycophenolate sodium (C2F9)

Time (min)	**Absorbance**	**Conc. (µg/mL)**	**Conc. in 900 mL (mg / mL)**	**Loss**	**ulativeloss**	**Cumulative drug released**	**Cumulative percentage drug released ***
0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0
75	0	0	0	0	0	0	0
90	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0
120	0	0	0	0	0	0	0
135	0.054	1.417	12.755	0	0	12.755	32.18+0.34
150	0.098	2.572	23.149	0.0141	0.0141	23.163	58.44+0.58
165	0.139	3.648	32.834	0.0257	0.0398	32.874	82.94+0.18
180	0.167	0.038	0.043	39.448	0.0364	0.076	99.72+0.46

***** Mean ± SD, *n* = 3

Table NO.06 *In vitro* drug release of Mycophenolate sodium (E1F9)

Time (min)	Absorbance	Conc. (µg/mL)	Conc. in 900 mL (mg / mL)	Loss	ulativeloss	Cumulative drug released	Cumulative percentage drug released *
0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0
75	0	0	0	0	0	0	0
90	0	0	0	0	0	0	0
105	0.03	0.8086	7.277	0	0	7.277	18.36+0.42
120	0.063	1.6981	15.283	0.0080	0.0080	15.291	38.58+0.22
135	0.104	2.7296	24.566	0.0169	0.0250	24.592	62.05+0.58
150	0.15	3.9370	35.433	0.0272	0.0523	35.485	89.53+0.39
165	0.164	4.3044	38.740	0.0393	0.0917	38.831	97.05

***** Mean ± SD, $n = 3$

CONCLUSION

- The Enteric coated tablets of Mycophenolate tablets were formulated and evaluated.
- The Formulation F3 and F9 (shows the best Disintegration test).
- This Formulations F3 and F9 were selected for Enteric coating and the polymers cellulose acetate phthalate and Eudragit-L were used for enteric coating.
- The Formulation C2F9 and E1F9 shows the better Dissolution results.
- However, compare to the E1F9, C2F9 shows better Dissolution n Enteric coating of tablets of Mycophenolate sodium

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REFERENCES

[1]. Chien,y.w,novel drug delivery system ,Marcel,Dekkaer,2nd Edition,Rev expand.50,139- 196
[2]. Essential of Medical Pharmacology by K.D Tripathi,6th edition ,Pg no 837-844
[3]. Shehata et al.Peadriatic transplant,01/08/2008
[4]. Goodman & gillman's,the pharmacological basis of therapeutics,11th edition,graw hills medical publication division 971-977,1866
[5]. Wolfgang Arns a , Stephan Breuer a , Somesh Choudhury b , Guy Taccard b , James Lee b , Vera Binder c , Jürgen Roettele c and Robert Schmouder b Merheim Medical Center, Cologne General Hospital, Cologne, Germany , b Novartis Pharmaceuticals, East Hanover, NJ, USA and c Novartis Pharma AG, Basel, Switzerland
[6]. Liberman & Leon Lachman,The theory & practice of Industrial Pharmacy,IIIrd edition ,verg hese Publication House,171,293.
[7]. Behrend, Matthias1; Braun, Felix2Source: Drugs, Volume 65, Number 8, 2005 , pp. 1037- 1050(14)Publisher: Adis International
[8]. The United State Pharmacopoeia 26/the national formulary, United State Pharmacopoeia, Conversion,INC 1615-1619.
[9]. Bilodeau JF, Montambault P, Wolff JL, Lemire J, Masse M Division of Transplantation, University of Maryland School of Medicine, Baltimore, MD 21201, USA. mcooper@smail.umaryland.edu.
[10]. Ansel, C.H., and Poppovich, N.G. (1995) Pharmaceutical Dosage Forms and Drug Delivery Systems, 6th Ed. B.I. Waverly Pvt.Ltd, New Delhi,213.
[11]. Aoki, S. (2005) Preparation composition containing acid unstable physiologically active compound and process for producing same, U.S Patent No. US 2005/0163846 A1.

[12]. Bruce, L.D., Hans-Ulrich Petereit, Thomas Beckert, James W., McGinity (2003). Properties of enteric coated sodium valproate pellets. International Journal of Pharmaceutics, 264(1-2): 85-96.
[13]. Lachman L, Lieberman H, Joseph L, The Theory and Practice of Industrial Pharmacy, 3rd Edn, Varghese Publishing House, Bombay, 1991, 293-373.
[14]. Kamble N, Chaudhari PS, Dr. Oswal RJ, "Innovations in tablet coating technology: a review", International Journal of Applied Biology and Pharmaceutical Technology, 2011, 2(1), 214-218.
[15]. Graham C, Pharmaceutical Coating Technology, 1st Edn, Taylor and Francis Publishers UK. 1995, 427-437.
[16]. Leopold CS, "Coated dosage form for colon specific drug delivery", Pharmaceutical Science Tech Today. 1999, 5, 197-204.
[17]. . Gohel M, Krishnakant G, Neelima R, "Assessment of Similarity Factor Using Different Weighting Approaches", Dissolution Technologies. 2005.
[18]. Paulo C, Manuel J, "Modeling and Comparison of dissolution profiles", European Journal of Pharmaceutical Science, 2001, 13, 123–133.
[19]. ICH, GUIDELINES Q1C, "Guidance for industry, stability testing of new dosage form" November 1996. http://www.ich.org/about/organisation-ofich/coopgroup/asean/topics-underharmonisation/article/stability-study.html.