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Research Article

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FORMULATION AND EVALUATION OF ASPIRIN DELAYED RELEASE TABLET

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ABSTRACT

The main aim of the work is to develop delayed release stable tablet formulation of Aspirin. The delayed release tablet is intended to release the drug after some delay or after tablet pass GI tract. The enteric coating is common example of this tablet. All enteric coated tablets are delayed release tablet but all delayed release tablet are not enteric coated tablets.[1] Aspirin delayed release tablet is used to increase bioavailability and to reduce risk of hospitalization for heart failure, coronary thrombosis deliver drug at a near constant rate for 24hr.[2,10] Keeping these factors in view it is aimed to formulate, evaluate and stabilize Aspirin (75mg) DR tablet to provide a controlled and predictable release of Aspirin and which is used in the treatment of Coronary Thrombosis (heart disease)[13], for Once in Day administration. The half life of Antiplatelet agent is 6 Hours which makes it suitable candidate for delayed release formulation. The present work aims to avoid degradation of drug in acidic environment of stomach. So due to enteric coating drug releases in to the small intestine so that drug gets larger surface area for absorption. Micro crystalline cellulose, maize starch, cross carmilose Sodium is a disintegrent used to prepare a blend for direct compaction method. Aspirin anti-platelet compounds which suppress or inhibit the cyclooxygenase enzyme which is responsible for the formation of thromboxane A_2, thus block the formation of thromboxane A_2. Thromboxane A_2 is a powerful activator of platelet aggregation.[3,12] Hence our present study was performed on these formulations as aspirin delayed release tablet.

Keywords: Delayed release tablet, direct compression method, Enteric coating tablet, Eudragit polymer-kollicoat MAE-30 DP, Hydroxy propyl methyl cellulose

INTRODUCTION

The present work is to develop a delayed release stable tablet formulation of Aspirin to increase bioavailability and to reduce risk of hospitalization for heart failure, coronary thrombosis deliver drug at a near constant rate for 24hr.

In case of aspirin[4,5], direct compression technique has been employed to compress the tablet, because the powder is highly moisture sensitive. Aspirin (75mg) DR tablet is to provide a controlled and predictable release of aspirin and which is used in the treatment of Coronary Thrombosis (heart disease)[8,9,11] for Once in Day administration. The delayed release tablet is intended to release the drug after some delay or after tablet pass GI tract. The enteric coating is common example of this tablet. All enteric coated tablets are delayed release tablet but all delayed release tablet are not enteric coated tablets. Aspirin delayed release tablet is used to increase bioavailability and to reduce risk of hospitalization for heart failure, coronary thrombosis deliver drug at a near constant rate for 24hr. In addition to its effects on pain, fever, and inflammation, aspirin also has an important inhibitory effect on platelets in the blood. This Antiplatelet effect is used to prevent blood clot formation inside arteries. Aspirin prevents blood from clotting by blocking the production by platelets of thromboxane A_2, the chemical that causes platelets to clump. It has an Antiplatelet effect by inhibiting the production of thromboxane.[6]

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MATERIALS AND METHODS

Aspirin were obtained as a gift sample from Andhra Sugar. Microcrystalline Cellulose, Maize Starch, Colloidal Silicon Dioxide, Talc, Stearic Acid, Croscarmellose sodium, HPMC - 15cps, PEG – 6000, Talcum, Titanium dioxide, Kollicoat MAE-30 DP, Triacetin, Talcum, Titanium dioxide were obtained as gift sample from Maneesh pharmaceutical, Mumbai.[7]

Preparation of Core Aspirin Tablets

The enteric coating tablet was prepared by direct compression method. The weighed quantity of aspirin, micro crystalline cellulose, maize starch were sieved through 40# size. The above shifted materials were mixed using planetary mixture for 10min. The shifted materials were lubricated with colloidal silicon dioxide, talc and stearic acid for 5 min octagonal blender. These blended materials were ready for compression.

The different formulas were given in table **1**.

Table 1. Formulation of aspirin core tablet F1–F3 batch

S.No	Ingredients	Amount (mg/ per tablet) Formulation No.		
		F1	F2	F3
1	Aspirin	80.0	80.0	80.0
2	Microcrystalline Cellulose	-	7.0	8.0
3	Maize Starch	14.5	7.0	7.0
4	Colloidal Silicon Dioxide	0.32	0.15	2.0
5	Talc	-	-	2.0
6	Stearic Acid	-	-	1.0
7	Croscarmellose sodium	-	-	2.0
8	Sodium lauryl sulphate	1.5 mg	1 mg	-
9	Lactose monohydrate	13.7 mg	6.85 mg	-
10	Average weight of tablet	110	102	102

From the above formula, formulation F3 batch has been selected due to its specification.

Procedure for preparation of Enteric coating solution

First take 150ml purified water, disperse the talc and titanium dioxide with continues stirring to form sol-A. Triacetin was dissolved in remaining quantity of water to form a (sol-B). Then weighed quantity of Kollicoat MAE-30 DP[12] was added in sol-B with continuous stirring for 5-10min. Finally sol-A was added in sol-B with continuous stirring (250 rpm) and filtered. Formulation for enteric coated tablet is shown in table **2**.

Table 2. Formulation of enteric coating aspirin tablet F3A – F3D batch

S. No.	Parameters	Formulation No.			
		F3A	F3B	F3C	F3D
1	Initial Weight of Tablets Bead	450 gm	480 gm	487 gm	492 gm
2	Kollicoat MAE 30 DP	50 %	50 %	50 %	50 %
3	Triacetin	2.25 %	2.25 %	2.25 %	2.25 %
4	Talcum	4 %	4 %	4 %	4 %
5	Titanium Dioxide	0.5 %	0.5 %	0.5 %	0.5 %
6	Purified Water	43.25%	43.25%	43.25%	43.25 %
7	% w/w Enteric coating Solution	21.75%	21.75%	21.75%	21.75%
8	Theoretical weight of tablets	481.5gm	489.1gm	494.5gm	500 gm
9	Final weight of tablets (Enteric Coated)	481 gm	488.8gm	493.3gm	498.3gm
10	% Build up	6.4 %	7.9 %	8.8 %	9.7 %
11	pH of coating solution	3.8	3.8	3.8	3.8

RESULTS

Evaluation of core tablets

The core tablets were evaluated for its thickness, friability, hardness and disintegration time. From the results it was found to be formulation F1 and F2 batches were failed to comply with specifications. Formulation F3 batch shown that all parameters complies with the limit.

Table 3. Evaluation of core tablets

Parameters	Formulation No.		
	F1	F2	F3
Average Weight of core tablet (mg)	109.3	101.2	102.4
Diameter (mm)	6.40	6.39	6.39
Thickness (mm)	3.22	3.20	3.24
Friability (%)	5.96	2.21	0.2
Hardness (Kg/cm^2)	1.5	1.7	3.25
Disintegration time (sec)	3	5	15

Evaluation for enteric coated tablets

In the Evaluation of enteric coated tablets, it was found that the F3A, F3B and F3C batches are failed because of low Disintegration time in 0.1N HCL. The Limit is tablet remain intact for 120 min. But in F3D batch enteric coated tablet, all parameter are pass as per BP specification are given in Table **4**.

Table 4. Evaluation of enteric coated tablets

Parameters	Formulation No.			
	F3A	F3B	F3C	F3D
Average Weight (mg)	111.19	112.12	113.2	114.8
Thickness (mm)	3.32	3.37	3.42	3.49
Disintegration time (min) (in 0.1 N HCl)	45-50 (Fail)	70-80 (Fail)	100-105 (Fail)	Pass
Disintegration time (sec) pH 6.8	N.A.	N.A.	N.A.	15
Dissolution (in 0.1N HCl)	N.A.	N.A.	N.A.	1.1 %
Dissolution (in phosphate buffer pH 6.8)	N.A.	N.A.	N.A.	96 %

Stability studies

The aspirin delayed release tablet was kept for stability at storage condition at 40°C / 75% RH for 30 Days. Description, Disintegration and dissolution for every storage condition were determined. Completing of all the study selected formulation F3D decided as a final product which complies with as per BP specification.

Table 5. Evaluation of enteric coated tablets after stability at 40ºC/75% RH.

Parameters	Formulation No.
	F3D
Disintegration time (min.) (in 0.1 N HCl) Limit(remain intact for 120 min)	Pass
Disintegration time (sec) (in phosphate buffer pH 6.8)	10-15
Dissolution (in 0.1N HCl)	0.4 %
Dissolution (in phosphate buffer pH 6.8)	95 %
Assay	100.53

DISCUSSION

The aim of the present work is to formulate delayed release aspirin tablet, to avoid degradation of drug in acidic environment of stomach. So due to enteric coating drug releases in to the small intestine so that drug gets larger surface area for absorption.

Under Preformulation study the organoleptic properties were complied with British pharmacopoeia (BP) specification. Physical properties such as loss on drying, angle of repose, compressibility, density, solution properties like solubility pH or color and clarity of the solution were evaluated. Results complied with the pharmacopoeia specification and identification for aspirin carried out by Infra Red (IR) spectral analysis.

Drug excipients compatibility study performed at 40°C /75% RH of 15 days. Micro crystalline cellulose, maize starch and cross carmelose Sodium were used to prepare a blend for direct compression method. The prepared blends were lubricated with silica colloidal anhydrous, talc, stearic acid. To protect the drug form degradation in acidic environment, final tablet formulation coated with pH dependant solubility polymer Kollicoat MAE 30 DP (Enteric coating polymer). Blends were compressed on tablet compression machine by using 6.5 mm punch. Finally optimized formulation for core tablet i.e. F3 is obtained. It gives all required parameters for core tablet. F3A-F3D formulations were selected for seal coating and finally enteric coating with Kollicoat MAE 30 DP having optimized polymer 10% coating.

These selected formulations were evaluated for tablet parameters i.e. Weight variation, thickness, hardness, disintegration in 0.1M HCl for 120 min and pH 6.8 phosphate buffer. In-vitro release in 0.1M HCl for 120 min & 6.8 pH phosphate buffer for 45 min.

Finally aspirin DR tablets were kept for its stability at different storage condition at 40°C / 75 %RH, for 30 days. Description, Disintegration and dissolution for every storage condition were determined. Completing of all the study selected formulation decided as a final product which complies with marketed product parameters.

CONCLUSION

From the above study it is concluded that, Aspirin Delayed Release 75 mg tablets were prepared by direct compression techniques, showed promising results when compared with marketed drug.

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