Development of USP Delayed Release Aspirin Tablets using Opadry® Enteric, Acrylic-Based Coating System

INTRODUCTION

Acetylsalicylic acid (aspirin) has been prescribed for a host of indications. Aspirin has analgesic, anti-inflammatory, and antipyretic properties. It acts as an inhibitor of the enzyme cyclo-oxygenase, which results in the direct inhibition of the biosynthesis of prostaglandins and thromboxanes from arachidonic acid. Aspirin also inhibits platelet aggregation.[1]

Because of its antiplatelet activity, low daily doses are used in preventive therapy for a variety of disorders. The most common adverse effect occurring with therapeutic doses of aspirin has been gastric irritation, the incidence of which increases with long-term use. Enteric protection is therefore, desirable in those taking daily aspirin therapy.

The objective of this study was to develop aspirin delayed release tablets that comply with USP requirements.

MATERIALS AND METHODS

Detailed composition of aspirin core tablets is shown in Table 1. Aspirin was used as supplied*. Starch1500®, partially pregelatinized maize starch, Vivapur 101 and stearic acid were passed through a British Standard Specifications (BSS) 36mesh (420µm) screen to break up any aggregates. Blending was carried out using the V-blender attachment of the Karnavati all purpose unit (HD 410AC, Karnavati Engineering).

Table 1- Composition of Aspirin Tablets

Material	Supplier	% w/w	mg/tablet	g/batch
Aspirin USP	Alta Laboratories Limited	50.0	81.00	500.00
Partially pregelatinized starch (Starch 1500)	Colorcon	20.0	32.40	200.00
Microcrystalline cellulose (Vivapur 101)	JRS Pharma	29.5	47.79	295.00
Stearic acid	Oleotec Limited	0.5	0.81	5.00

* Total retention on:
20 mesh (850 microns): 6.20%
40 mesh (420 microns): 70.50%
100 mesh (150 microns): 97.40%

TABLET MANUFACTURE

Aspirin tablets (162mg) were manufactured using an 8 station Rimek Mini-Press- II SF (Karnavati, India), fitted with 7 mm standard concave tooling. Tableting was carried out at 20 rpm at a compression force of 13kN (337.8 MPa).

TABLET COATING

Seal-coating

Aspirin tablets were seal-coated to 2% weight gain (wg) in a Bectochem conventional coating pan (12 inch pan diameter) using Opadry®, complete film coating system, 03K clear, (reconstituted at 6% solids), in a hydro-alcoholic solvent system 85:15 (ethanol:water) using a Schlick 970 spray gun. Coating process parameters are listed in Table 2.

Enteric coating

Seal-coated aspirin tablets were enteric coated using Opadry® Enteric, acrylic-based coating system, 94O white. Opadry Enteric coating dispersion was prepared as outlined in the 'Preparation and Use Guidelines' for Opadry Enteric-94 Series, in a hydro-alcoholic solvent system 85:15 (ethanol:water).[2] Coating was carried out to a 9% wg. Coating process parameters are listed in Table 2.

Table 2- Coating Process Parameters

	Seal-coating	Enteric coating
Tablet charge (g)	500	500
Product temperature (^{o}C)	32-34	29-31
Fluid delivery rate (g/min)	5-6	5-6
Pan speed (rpm)	16-18	16-18
Atomization air pressure (bar)	1.5	1.5
Air flow (m^3/h)	140	140

TABLET TESTING

Tablet physical properties testing

Breaking force of the uncoated, seal-coated and enteric coated tablets was measured using a hardness tester (Pharmatest, India). Friability was measured using a USP compliant friabilator (Electrolab, India).

Assay

Assay was determined in accordance with the USP 30/NF 25 monograph for aspirin delayed release tablets. The USP specifies that aspirin delayed release tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of aspirin.

Uniformity of dosage units

Uniformity of dosage units for coated tablets was carried out in accordance with the USP General Chapter: <905> Uniformity of Dosage Units.[3] The uniformity of dosage units was demonstrated by the *weight variation* method. The requirements of dosage uniformity are met if the calculated *acceptance value* (AV) is less than the *maximum allowed acceptance value* (L1) of the content.

Dissolution testing

Dissolution testing was carried out in accordance with the USP 30/NF 25 monograph for aspirin delayed release tablets. Drug release was determined using a USP compliant automated dissolution bath (Erweka DT 800), Apparatus I (baskets) at 100 rpm. At the end of the acid stage, (2 hours in 0.1 N hydrochloric acid), an aliquot was withdrawn and tested for content of aspirin released. The specification for the acid phase is not more than 10% aspirin dissolved. The acid was then drained from the vessel, and replaced with pH 6.8 phosphate buffer. Sample aliquots were withdrawn from the buffer phase (pH 6.8 phosphate buffer) at 30, 45, 60 and 90 minutes, and analyzed for the amount of aspirin dissolved. The specification for the buffer phase is not less than 80% drug dissolved after 90 minutes.

Test for free salicylic acid

The test was carried out in accordance with the USP 30/NF 25 monograph for aspirin delayed release tablets. The USP specifies a limit of not more than 3.0% for delayed release tablets.

Stability testing

Enteric coated tablets were packaged in 100cc HDPE bottles (385 tablets per bottle, with/without desiccant) and stored for 6 months at accelerated conditions of 40^{o}C/75%RH.

RESULTS AND DISCUSSION

Physical characterization

Good physical properties were obtained for compressed tablets. Enteric coated tablets had good physical appearance. Tablet breaking force increased subsequent to seal-coating and enteric coating of the aspirin tablets (Table 3).

Table 3 - Physical Properties of Aspirin tablets (n=10)

Tablet Properties	Tablet parameters		
	Core	Seal-coated	Enteric coated
Thickness (mm± S.D)	3.94 ± 0.01	3.96 ± 0.01	3.97 ± 0.04
Weight (mg± S.D)	161 ± 2.3	162 ± 2.5	175 ± 4.5
Crushing Strength (kP± S.D)	8.6 ± 0.8	13.1 ± 1.1	16.5 ± 1.3
Tensile Strength (MPa ± S.D)	2.5 ± 0.52	3.7 ± 0.43	4.7 ± 0.43
Friability (%)	0.05	0.00	0.00

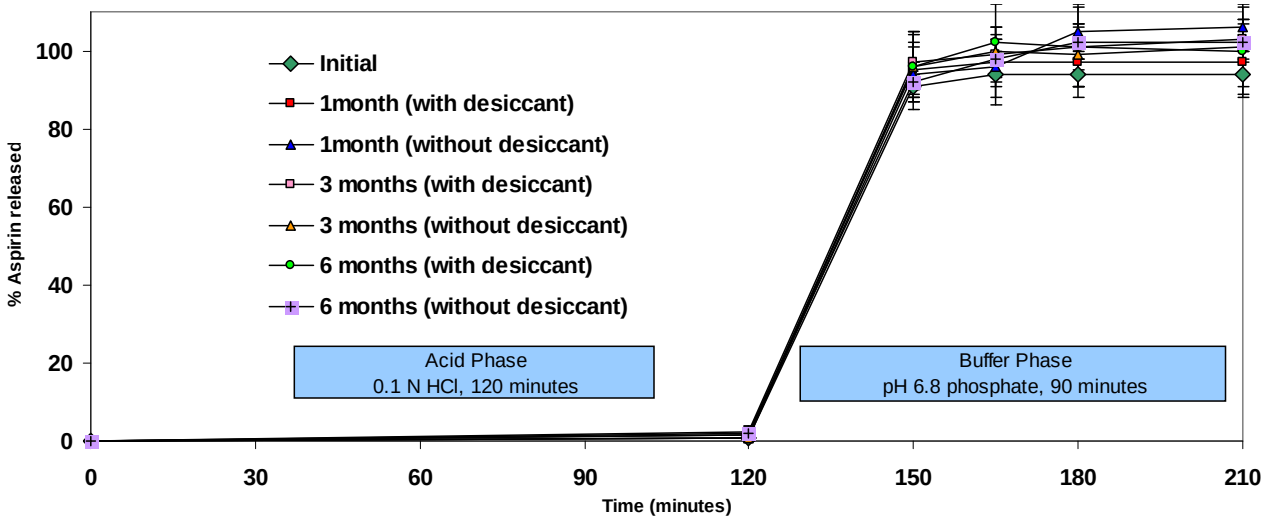
Uniformity of dosage units

An *acceptance value* (AV) of 7.0 was obtained for enteric coated tablets. The requirements of dosage uniformity were met, as the AV was less than the *maximum allowed acceptance value* which is 15.

Dissolution testing

Enteric coated tablets passed the acid stage of the dissolution test, with no release of aspirin after 2 hours in 0.1N HCl. Greater than 80% (Q+5%) aspirin was released in the buffer phase within 30 minutes (Figure 1).

Figure 1 – Dissolution Profile for Enteric Coated Aspirin Tablets



Assay

Enteric coated tablets were assayed and found to contain 100.8% of the labeled amount of aspirin (Figure 2).

Free salicylic acid

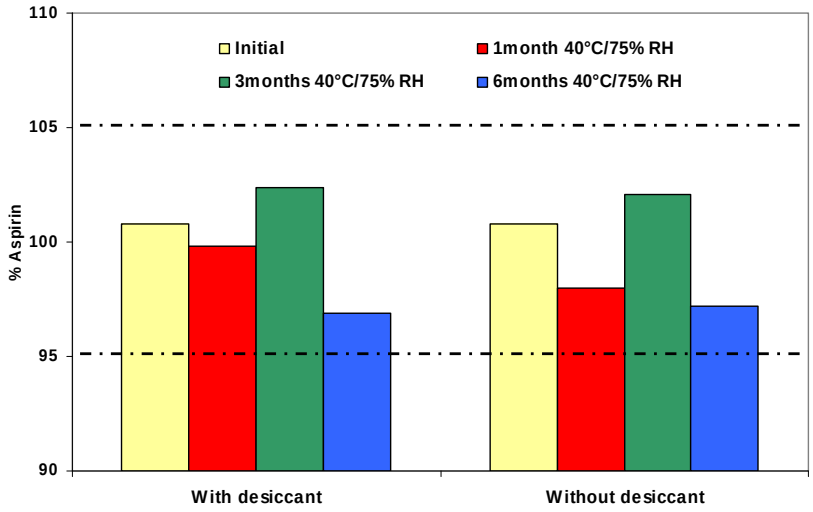
Free salicylic acid content was determined and found to be 0%.

Stability

Tablet assay, dissolution and free salicylic acid were determined for coated tablets after 6 months storage at accelerated temperature and humidity conditions (40^{o}C/75%RH).

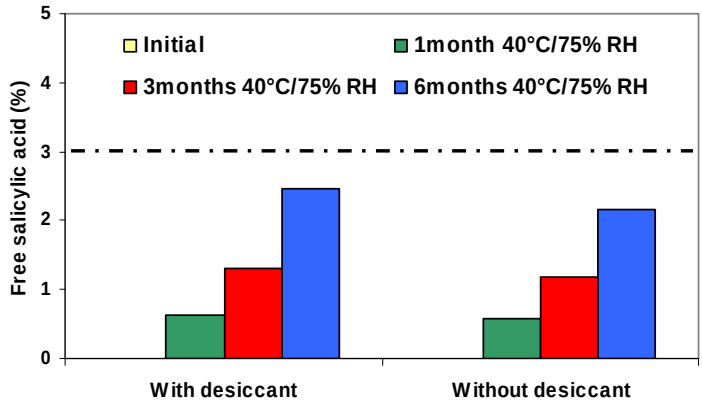
Assay of coated tablets stored at 6 months 40^{o}C/75%RH met the USP requirements (95- 105%) of the labeled amount of aspirin.

Figure 2 – Assay before and after storage at 6 months at 40°C/75%RH



Free salicylic acid content was less than 2.5% after 6 months of storage at accelerated conditions (Figure 3).

Figure 3 – Free salicylic acid before and after storage at 6 months at 40°C/75%RH



Minimal change was observed in dissolution results (Figure 1) as compared to the initial results obtained. The enteric coating provided good protection in acid phase and greater than 80% release in 30 minutes even after 6 months at 40°C/75%RH.

CONCLUSION

A delayed release aspirin 81mg tablet formulation was developed using Opadry Enteric. The core formulation yielded mechanically strong tablets with low weight variation. The enteric coated formulation met the USP specifications for aspirin delayed release tablets, and exhibited excellent accelerated storage stability.

REFERENCES

1. Martindale, Pharmaceutical Press, London, UK, 1999, p. 18.
2. Opadry Enteric -94 Series, Preparation and Use Guidelines, Colorcon Technical Literature.
3. United States Pharmacopoeia 30/National Formulary 25 Online, 2007.

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