Startab®
Directly Compressible Starch

Colorcon®

Impact of Core Excipient Selection to Improve the Stability of a Moisture Sensitive Drug, Acetylsalicylic Acid

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Introduction

Acetylsalicylic acid (ASA) has analgesic, anti-inflammatory, and antipyretic properties used to treat and prevent heart attacks, strokes, and heart-related chest pain (angina). The most common adverse effect with long term therapy of ASA is gastric irritation, hence, enteric protection is desirable. ASA is known to undergo hydrolytic degradation to acetic acid and salicylic acid in the presence of moisture and elevated temperature.[1] These challenges can be overcome by choosing the appropriate excipients that have low water activity and can provide stability from moisture-induced degradation. StarTab®, Directly Compressible Starch, shows excellent flow and superior compressibility on high-speed tablet press machines.[2] The aim of this work was to study the impact of StarTab concentration, as a diluent with low water activity and good compressibility, on stability of ASA delayed release (DR) tablet formulations.

Methods

Three different ASA (75 mg) core formulations with target tablet weight of 182 mg (Table 1), were prepared using direct compression with varying concentrations of StarTab (Formulations 1, 2 and 3 with 23%, 43% and 58%, respectively) along with microcrystalline cellulose and stearic acid (Figure 1).

Coating of Tablets:

All tablets were seal-coated with a clear HPMC-based Opadry® compete film coating system 03K at 2% weight gain using 6% w/w solids in IPA: water (88:12 ratio). The seal-coated tablets were subsequently enteric coated with methacrylic acid-ethyl acrylate copolymer (1:1) based Acryl-EZE® 93O enteric coating system at 10% weight gain using 20% w/w solids in water (Table 2). Tablet coating was performed in a 10.5" perforated coating pan (O'HARA Labcoat M5), using a 700 g batch size.

Figure 1: Flowchart for Manufacturing of ASA Core Tablets using Direct Compression

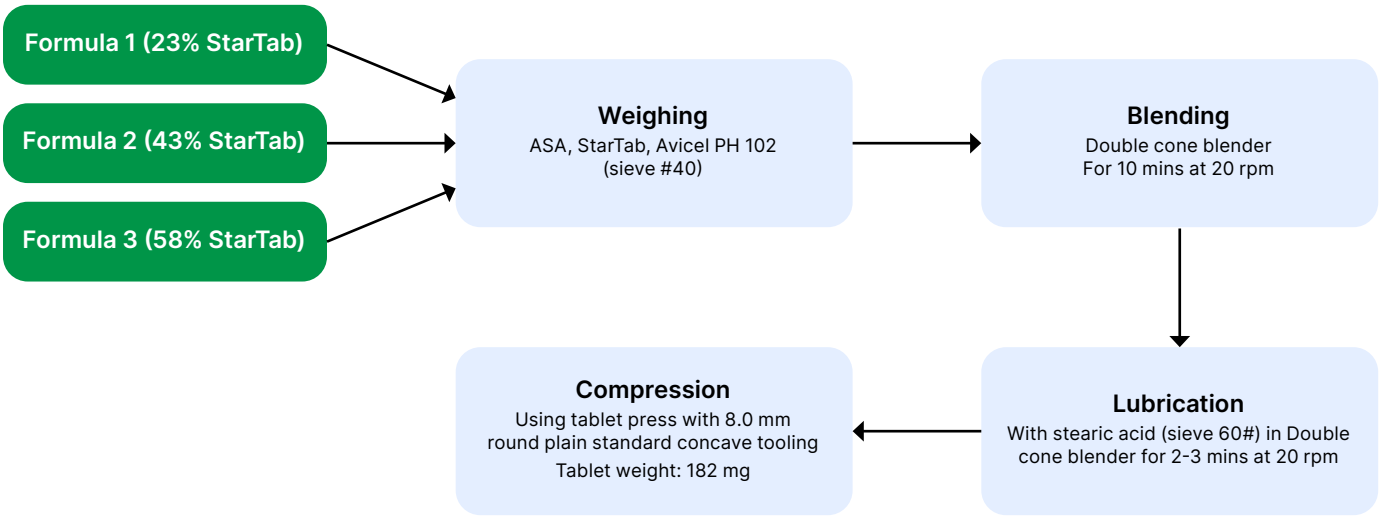


Table 1. Composition of ASA Tablets

Ingredients	Supplier	Trial 1		Trial 2		Trial 3	
		% w/w	mg/tab	% w/w	mg/tab	% w/w	mg/tab
***ASA IP**	Alta Laboratories	41.2	75.0	41.2	75.0	41.2	75.0
StarTab	Colorcon	23.2	42.3	43.2	78.6	58.0	105.6
Microcrystalline cellulose, Avicel pH 102	IFF	34.8	63.3	14.8	26.9	NA	NA
Stearic acid	Arihant Innochem Pvt Ltd	0.8	1.4	0.8	1.4	0.8	1.4
Total		100.0	182.0	100.0	182.0	100.0	182.0

Table 2. Coating Process Parameters

Parameter	Seal-Coat	Enteric Coat
Weight gain, % w/w	2.0	10.0
Atomization air pressure, bar	0.6-0.7	1.0-1.1
Pattern air pressure, bar	0.4-0.5	1.0-1.1
Pan speed, rpm	15	14
Inlet air temperature, ˚C	37-39	37-40
Exhaust air temperature, ˚C	30-33	31-33
Bed temperature, ˚C	33-34	32-34
Air volume, m^3/h	118	124
Spray rate, g/min	7-8	2-3

Enteric Performance Testing:

Enteric performance testing of coated tablets (n=6) was evaluated using a USP disintegration bath (Electrolab, ED-2L) containing either 0.1N HCl for 2h at 37 ± 2˚C. The tablets were observed at the end of acid stage for any defects (swelling/cracking). The percent liquid uptake of the tablets was calculated. The intact tablets were subsequently subjected in the disintegration apparatus using pH 6.8 phosphate buffer, at 37.0˚C. The time taken for all the tablets to disintegrate was recorded.

Assay, Impurities and Dissolution:

ASA DR Tablets were evaluated for assay and free salicylic acid (FSA) impurities as per USP monograph. Drug release was determined using the following two different sets of dissolution media:

Acid Stage: 1000 mL of 0.1N HCl, 37.0 ±0.5ºC, using apparatus I at 100 rpm for 120 mins.

Buffer Stage: 900 mL of phosphate buffer pH 6.8, 37.0 ±0.5ºC, using apparatus I at 100 rpm for 90 min.

At the end of the acid stage (120 min), dissolution testing was continued with buffer stage and sample aliquots were withdrawn and analyzed spectrophotometrically for ASA released at 280 nm and 265 nm, respectively.

Stability Testing:

Coated tablets were packaged in 75 cc HDPE bottles, sealed and screw-capped, and subjected to stability evaluation for 6 months at 30°C/65% RH and 40°C/75% RH storage. Stability of enteric coated tablets was monitored by testing drug release, assay, impurities, % LOD and enteric performance as described above.

Results

Powder blends of all three formulations showed good flow on the rotary tablet press, producing tablets with low weight variation, desired hardness (8-9 kP), thickness and low friability (0.34%) with faster disintegration time (< 1 min).

ASA DR tablet formulations 2 and 3 at initial and accelerated stability conditions for 6M remained intact (acid uptake < 10%) during the acid stage (0.1N HCl) up to 120 min each, followed by rapid disintegration (< 11 min) in the buffer stage (phosphate buffer pH 6.8). All three formulations of ASA DR tablets, subjected to dissolution tests, showed no significant difference in drug release up to 120 min in acid stage, while more than 95% of the drug was released in buffer stage (phosphate buffer pH 6.8) within 90 min at initial, as well as at 6M accelerated stability storage. The dissolution profile of Trial 3 tablets is shown in Figure 2. Assay and FSA content of formulations 2 and 3 were found to be >95% and <3.0%, respectively, after 6M accelerated stability condition. However, tablets of formulation 1, with a relatively lower proportion of StarTab, showed lower assay (~93%) and higher FSA values (7.5%) at 6M accelerated stability condition (Figure 3). During the stability study at 6M, LOD for Formulations 1,2, and 3 remained stable at 4.20%, 4.71% and 5.44% respectively, showing no significant changes from the initial values of 3.95%, 4.89% and 5.99%.

Figure 2: Dissolution Profile of ASA DR tablets (Trial 3: 58.0% StarTab)

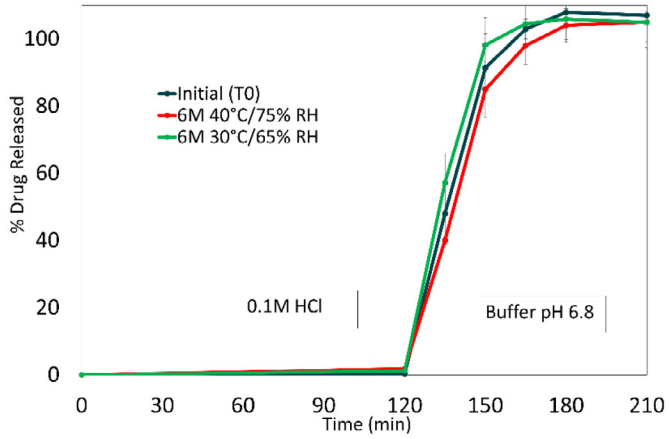
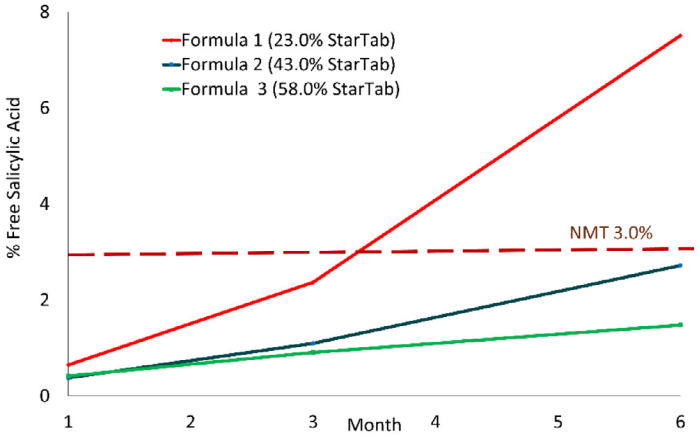


Figure 3: FSA Content of ASA DR Tablets at 40ºC/75% RH Conditions



Conclusions

ASA DR formulations were successfully prepared using a direct compression method, with varying concentrations of StarTab in the core, followed by Opadry 03K clear as the seal-coat and Acryl-EZE 93O as the enteric coating. Formulation 3, which contained a higher percentage of StarTab (58%), showed the lowest impurity (FSA) generation following 6 months exposure to accelerated stability conditions and no impact on dissolution and % assay; demonstrating the ability of StarTab to improve stability of ASA tablets.

References

1. Aspirin - Wikipedia
2. https://www.colorcon.com/search/item/3975-startab-product-brochure