Study of the Deterioration of Aspirin in the Presence of Various Excipients

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Abstract

Aspirin is a non steroidal anti-inflammatory drug. Hydrolysis is the main stability threat for aspirin tablets. Aspirin is an ester compound and it easily gets hydrolyzed in the presence of moisture to form salicylic acid. This study was carried out to determine the effects of excipients on aspirin hydrolysis. For this purpose aspirin was mixed with 34 different excipients and subjected to accelerated stability test conditions. Free salicylic acid present in each sample was determined after 21 days. It was found that dried maize starch, lactose monohydrate, anhydrous lactose, sodium Lauryl Sulphate (SLS) produced a low percentage of salicylic acid. Three new aspirin formulations were developed using the above excipients. In addition, microwave induced aspirin synthesis was attempted to enhance the yield of aspirin synthesis.

1. Introduction

In a formulation, drugs have intimate contact with one or more excipients, which can affect drug stability. Therefore knowledge of drug excipient interaction is essential for appropriate excipient selection. Moisture often plays a key role in the physical and chemical stability of a dosage form. The most common effect of moisture on chemical stability is hydrolysis; aspirin is a well-known example [1]. Aspirin-excipient interactions have been studied in the literature [2], however in tablet manufacturing drug excipient interaction causes aspirin hydrolysis. In this study based on aspirin-excipients interaction results, development of new formulations for aspirin 300 mg tablets (150 mg x 2) was attempted.

Recently, there has been a growing interest in the use of microwave technology for organic synthesis [3]. It offers certain advantages such as shorter reaction time, high yield and reduction of secondary product. Microwave induced aspirin synthesis was also attempted to enhance the yield of aspirin synthesis during this study.

2. Experiment

2.1 Study of drug-excipient interactions

Aspirin-excipient binary samples were prepared by mixing same amount of aspirin with different amount of excipients. This was done for 34 excipients. All the samples were kept in stability oven (60°C, 45% Relative humidity, and 21 days) for stability studies. Free salicylic acid amount present in every sample were determined after 21 days using HPLC, according to the USP method.

The HPLC system (Agilent, 1100 series, German) equipped with a UV detector and a 4.0 mm x 30 cm C_{18} column was used for HPLC analysis. UV absorbance was measured at 280 nm. Acetonitrile and pH 3.4 buffer (15:85) mixture was used as the HPLC solvent. The flow rate of the mobile phase was maintained at 2 mL/minute. Attempts were made to improve the retention time of the aforementioned USP HPLC method during this study.

2.2 Study of particle size of aspirin on hydrolysis

Aspirin was passed through the sieve shaker having sieves (mesh 40, 60, 80,100,120,150 and 200) and aspirin samples were collected from mesh 60,120 and 200. Collected aspirin sample were mixed with selected excipients in a glass sample bottle. After the stability studies, the amount of free salicylic acid present in every sample was analyzed.

2.3 Development of new formulation for aspirin 300 mg (150 mg x 2) tablets

Three new formulations were developed for direct compression aspirin 300 mg (150 mg x 2) BP tablets by changing the amount of dried maize starch, lactose monohydrate, anhydrous lactose and microcrystalline cellulose (MCC, low moisture). The above formulations of tablets were evaluated with respect to various quality parameters such as, powder properties and tablet properties.

Table 1: Details of developed formulations

Ingredients	Formulations (mg)		
	1	2	3
Aspirin	300.0	300.0	300.0
Sodium lauryl sulphate (SLS)	1.0	1.0	1.0
Lactose monohydrate	60.0	-	39.0
Anhydrous lactose	-	60.0	-
Maize starch (dried)	39.0	24.0	30.0
Microcrystalline cellulose (low moisture)	-	15.0	30.0

Powder properties and tablet properties were tested for all 3 formulations.

2.4 Synthesis of aspirin using microwave

Salicylic acid (200 mg) and acetic anhydride (3 mL) were added to a beaker. Then five drops of concentrated H_2SO_4 was added as a catalyst. Reaction mixture was placed in a microwave oven for different time intervals at different power settings. Thereafter the crude product was recrystallized using water: ethanol mixture (4.5:0.5).

3. Results and Discussion

3.1 Study of drug-excipient interactions

The free salicylic acid present in aspirin-excipient binary mixtures were statistically analyzed to identify the best excipient for aspirin tablets by comparing with the free salicylic acid present in aspirin without an excipient. Out of all binders, dried maize starch contributes to form low percentage of salicylic acid (0.058%). Out of all fillers, lactose monohydrate and anhydrous lactose were the best (0.055% and0.062%). In the case of lubricants, Sodium Lauryl Sulphate (SLS) contribute to form low percentage of salicylic acid (0.163%).

When followed the USP-HPLC method, it took 26 minutes in order to obtain both salicylic acid, aspirin. During our study, the retention times were improved and both compounds were obtained within 12 minutes by allowing the HPLC to pump the two solvents; acetonitrile and buffer from two different solvent bottles.

3.2 Study of particle size of aspirin on hydrolysis

According to the results, it is difficult to come to a conclusion, on how the aspirin particle size affects the rate of hydrolysis.

3.3 Development of new formulation for aspirin 300 mg (150 mg x 2) tablets

The powder properties and tablet properties of all three formulations are tabulated below.

Table 2: Results of powder properties

Formulation	Powder property	
	Angle of repose	Compressibility index (%)
1	36.3	28.5
2	34.6	23.0
3	38.9	30.0

Table 3: Summary of tablet properties (before stability test)

Formulation	Tablet properties					
	Hardness (Kp)	% friability	Disintegration time (min)	Dissolution (average)	% Free salicylic	% of aspirin
1	3.9	1.4	0.2	113.056	0.07	93.9
2	4.2	0.9	0.3	118.880	0.09	94.4
3	3.9	1.0	0.1	105.005	0.07	92.6

Table 4: Summary of tablet properties (after stability test)

Formulation	Tablet properties					
	Hardness (Kp)	% friability	Disintegration time (min)	Dissolution	% Free salicylic	% of aspirin
1	4.8	1.1	0.5	115.282	0.09	91.1
2	6.5	0.9	0.5	102.778	0.09	92.8
3	6.1	0.8	0.2	104.576	0.08	90.7

According to the results formulation number 2, which contains dried maize starch (24%), anhydrous lactose (60%), MCC/low moisture (15%) and SLS (1%) met all the requirements suitable for proper aspirin tablet.

3.4 Synthesis of aspirin using microwave

According to the results, the best power setting for the microwave synthesis is 320W and the time required to give the best yield is 30 seconds. Under these conditions, microwave method gave comparatively higher yield (73%) of product (aspirin) than the conventional heating methods (70%) within shorter reaction time. However the purity of the product seems to be affected by the microwave radiation as the colour of the product is pale yellow.

References

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