

QUALITY EVALUATION OF GASTRORESISTENT TABLETS OF ACETYLSALICYLIC ACID

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Abstract

INTRODUCTION: Acetylsalicylic acid (aspirin - ASA) is an important drug of nonsteroidal anti-inflammatory group with analgesic, antipyretic and anti-inflammatory properties. Delayed-release tablets are used to increase the bioavailability and reduce the risk of hospitalization of cardiac diseases. The efficacy of aspirin in preventing myocardial infarction is associated with preventing the formation of thrombi by slowing the aggregation of blood cells. Six types of 100 mg acetylsalicylic acid tablets are registered in the Albanian market and in the reimbursement list. The aim of this investigation was the quality evaluation of gastroresistent tablets of aspirin 100 mg and the estimation of dissolution profiles.

MATERIALS AND METHODS: The methodology used was based on the monograph of British Pharmacopeia 2007. Tablets control underwent organoleptic (eye inspection), physical and chemical. The in vitro dissolution studies were carried out in the dissolution apparatus, which was initially left for 2 hours in 0.1M HCl solution and then for 90 min at pH 6.8 phosphate buffer medium. Samples taken at various times were analyzed in UV-VIS spectrophotometer at 276 nm using 0.1M hydrochloric acid as reference cell and at 265 nm for the phosphate buffer medium, respectively. Four brands of delayed release tablets 100 mg, used for analysis, were collected from Albanian market.

RESULTS AND CONCLUSIONS: There was no significant change in the measurement of these parameters for the four dosage forms with reference to British Pharmacopoeia (BP) values. From the dissolution profiles obtained, the dissolution of drug in medium pH 6.8 was achieved within the first minutes on most tablets.

Key-words: Acetylsalicylic acid, delayed release tablets, dissolution, dissolution apparatus

Introduction

Acetyl Salicylic Acid (ASA) or Aspirin (Figure 1) is one of the oldest and the most commonly used non steroidal anti-inflammatory drugs (NSAID). It is an effective analgesic, anti-inflammatory, anti-thrombotic and antipyretic agent that primarily acts by permanently inactivating the cyclooxygenase (COX)

mediated activities of prostaglandins through irreversible binding unlike other NSAIDs, which are reversible inhibitors. Cyclooxygenase is required for prostaglandin and thromboxane synthesis. Aspirin acts as an acetylating agent where an acetyl group is

covalently attached to a serine residue in the active site of the COX enzyme [1,2,3].

Aspirin's efficacy in preventing Myocardial Infarction is related to preventing thrombus formation by decreasing platelet aggregation [4].

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 A₂, the chemical that causes platelets to clump. It has an antiplatelet effect by inhibiting the production of thromboxane [1].

Aspirin often causes acute gastric mucosal damage that can be seen endoscopically or assessed indirectly (for example, by measuring increased gastrointestinal blood loss). The occurrence of most adverse effects is apparently related to the dose administered. This dose-response effect, evident in both endoscopic and

microbleeding studies done after acute or short-term aspirin administration, is also associated with the risk of developing chronic gastric ulcer [5].

In the Albanian market and in the reimbursement list are registered six types of tablets 100 mg of acetylsalicylic acid. The aim of this investigation was the quality evaluation of gastro-resistant tablets of aspirin 100 mg and the estimation of dissolution profiles.

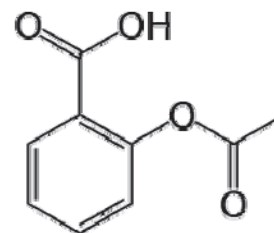


Figure 1. Structure of Acetyl Salicylic Acid (ASA).

Materials And Methods

Four different brands of gastroresistant ASA100 mg tablets were purchased from the retail pharmacy and were signed as samples M1, M2, M3 and M4. All the reagents used were purchased by Sigma Aldrich Company.

Equipments

Tablet Hardness- Guoming YD-2; Disintegration Test Apparatus - Guoming YD-2; Dissolution Test Apparatus - Guoming YD-2; Spectrophotometer UV-VIS model UV765; quartz cuvettes, 1 cm.

Methods

For all the tablets selected, the tests of identity, uniformity of weight and diameter, crushing strength, disintegration were done, and also the assay for the content of active ingredients by iodometry and spectroscopy as described in the British Pharmacopoeia [9] and literature [6,7,8,10]. All the

assessments were triplet and the results presented are the average of them.

Also all the tablets underwent in vitro dissolution study using USP apparatus type II.

Data analysis

Data for hardness, diameter, weight uniformity test, disintegration and content uniformity of the tablets were analyzed by determining the mean and standard deviation.

Hardness

Hardness of the tablet was measured using Tablet Hardness- Guoming YD-2tester. Seven tablets of each brand were randomly selected and the hardness of the tablets was determined (n=7).

Diameter

Random samples of 10 tablets were selected for each brand and their diameter was calculated in centimeters with the help of micrometer.

Uniformity of mass

The weights of ten tablets were determined individually using an analytical balance. The average tablet weight and standard deviation were calculated and compared with the permissible limits [7].

Identification

A quantity of powder equivalent to 0.3 g of Aspirin was boiled for 2 to 3 minutes with 10 ml of 5M sodium hydroxide, was cooled, and adding an excess of 1M sulphuric acid, a crystalline precipitate was produced. To a solution of the precipitate in water, iron (III) chloride solution [9] was added.

Disintegration

For this test, the disintegration apparatus with two baskets was used. The 900mL beakers were first filled with hydrochloric acid 0.1 M and were kept at $37\pm 0.5^{\circ}\text{C}$ for two hours. Six tablets of each brand were selected and placed in each of the cylindrical tubes of the basket without discs. After 120 minutes the medium was changed with phosphate buffer solution pH 6.8. Discs were used to avoid the floating of tablets while tube moved upwards and downwards in water. The time taken to break each tablet into small particles and pass out through the mesh at the bottom of the tube was recorded [9].

Assay

20 tablets of aspirin were weighed and pulverized and an amount equivalent to 100 mg of Aspirin was transferred to a 250 ml Erlenmeyer flask, in which 2 ml ethanol 70 % and 5 mL of 0.5 M sodium hydroxide was added. The mixture obtained was gently mixed and was left to stand for 60 minutes. The base excess was titrated with 0.5 M hydrochloric acid, using phenolphthalein as indicator. The same procedure was performed to the blank test. Each ml of 0.5 M

sodium hydroxide is equivalent to 45.040 mg of Aspirin [10,11].

Dissolution test

The dissolution was carried out using first as the medium 1000 ml of 0.1M hydrochloric acid and rotating the basket at 100 revolutions per minute. After 2 hours, a sample of the medium was withdrawn, was filtrated and the absorbance of the filtrate was measured at 276 nm using 0.1M hydrochloric acid in the reference cell. The absorbance of a suitable solution of standard aspirin in 0.1M hydrochloric acid was measured and the total content of aspirin in the medium was calculated, using the declared content of ASA in standard aspirin.

After this procedure the medium in the baskets was replaced with 900 ml of mixed phosphate buffer pH 6.8, previously held at 36.5° to 37.5° . After 45 minutes, a sample of the medium and filter was withdrawn. Immediately the absorbance of the filtrate was measured, at 265 nm using dissolution medium in the reference cell. Accordingly, the absorbance of a suitable solution of standard aspirin in the dissolution medium was measured, and the total content of aspirin [9, 12] was calculated.

Dissolution profile

The dissolution profile was obtained using the same methodology described for the dissolution test, but this test was performed for 45 minutes with aliquots collection at 10, 20, and 45 minutes. In each sample, a 10 ml aliquot of dissolution medium was removed, this volume being immediately replaced [10].

Results And Discussion

All the trial samples (M1, M2, M3 and M4) were evaluated using pharmacopoeial (they have undergone visual inspection, thickness, disintegration

and hardness tests) and nonpharmacopoeial tests (identification, assay and dissolution tests).

The results obtained for each sample after the hardness test, diameter and uniformity of mass measurements are given at the table 1.

Table 1: Parameters of ASA 100 mg tablets

Products	Thickness/mm										
M1	85.2	82.5	82.7	82.9	82.4	85.2	85.2	88.2	82.7	82.9	
M2	75.4	75.3	75.4	75.3	85.5	75.5	75.3	75.4	75.4	75.3	
M3	75.8	79.1	75.8	71.6	72.4	71.4	71.2	79.3	71.9	72.5	
M4	87.6	88.4	87.4	88.3	88.4	87.6	87.9	87.5	88.2	87.9	
	Hardness/N										
M1	126.2	112.5	103.5	128.2	119.1	99.7	101.5	114.7	127.5	130.1	
M2	52.8	51.2	53.0	49.9	50.8	52.4	51.9	51.5	52.6	52.2	
M3	78.6	77.9	80.2	79.1	78.2	77.8	81.1	78.6	75.9	77.5	
M4	72.2	71.8	70.9	72.0	73.1	71.5	72.2	71.2	73.0	72.2	
	Weight variations										σ $\sigma = aw \pm 7.5\%$
M1	0,2156	0,2156	0,2156	0,2156	0,2156	0,2156	0,2156	0,2156	0,2156	0,2156]0.14086;0.29086[
M2	0.1305	0.1305	0.1305	0.1305	0.1305	0.1305	0.1305	0.1305	0.1305	0.1305]1,2089;1,3589[
M3	0.1482	0.1482	0.1482	0.1482	0.1482	0.1482	0.1482	0.1482	0.1482	0.1482]0,07292;0,22292[
M4	0.1369	0.1369	0.1369	0.1369	0.1369	0.1369	0.1369	0.1369	0.1369	0.1369]0,06109;0,21109[

After the physical tests, the tablets were subjected to chemical tests that include identification, assay, disintegration and dissolution.

Identification test

After the above procedure, a deep violet color is produced in the solution indicating the presence of the aspirin for each sample.

Test of Disintegration

The ASA gastro - resistant tablets according to monographs BP 2007 specify the time of disintegration, 2 h in HCl 0.1 M at 37°C, in the disintegration apparatus. There ought to be no cracking or coating break, and after that the tablets are put in phosphate buffer, pH 6.8 at the same temperature for 1 hour. Most of the tested tablets were disintegrated within ten minutes.

Assay

The drug content was found to be between the values 98% to 104%, values which are within the pharmacopeal limits. The amount of acetylsalicylic acid is shown for each sample in the table 2 below:

Table 2: The drug content

Samples	The amount of ASA %
M1	102
M2	104
M3	98
M4	104

Dissolution test

Samples were taken from both media, and the total content of released aspirin in percentage has been calculated, relying on the obtained absorbance values, first in the HCl medium, $\lambda = 276\text{nm}$, and in buffer phosphate medium, $\lambda = 265\text{ nm}$ in the end of 45th minute

The quantity of released aspirin in acidic environment does not surpass 5% of the declared (stated) quantity on the label of the drug container. The obtained values are summarily presented in the graphs of fig. 2

Table 3: The percentage of ASA release in each medium

Samples	% release in HCl 0.1 M	% release in phosphate buffer pH 6.8
M1	3.02%	83.7%
M2	2.06%	82.3%
M3	1.86%	85.1%
M4	2.60%	83.2%

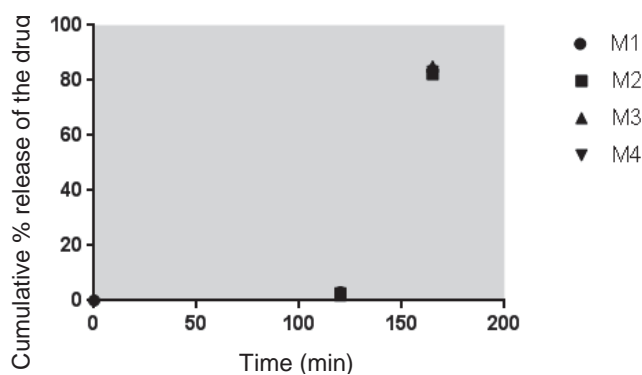


Figure 2: Graph of cumulative release of ASA in each medium HCl 0.1 M and buffer phosphate pH 6.8

From the graph we can conclude that each sample of the tablets has approximately the same cumulative percentage in the 45th minute, in buffer phosphate medium.

Dissolution profile

The obtained values of the cumulative quantity of the released drug after 10, 20 and 45 minutes are presented in the bottom graph (Fig.2). From this graph we may conclude that the larger quantity of released ASA occurred in the 20th minute for each of samples selected for analysis, and the higher percentage released was that of sample M2

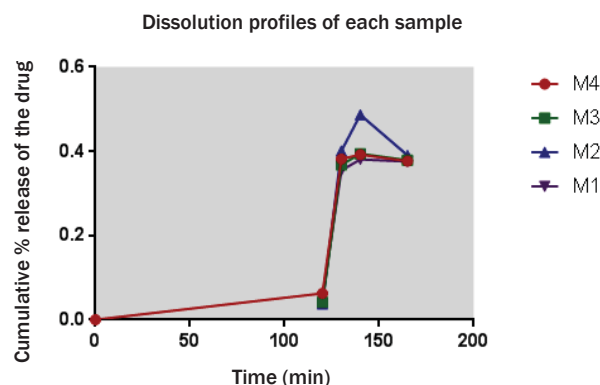


Figure 3: Dissolution profiles of ASA delayed release tablets in each medium HCl 0.1 M and buffer phosphate pH 6.8

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