Original Article

Stability evaluation of Acetylsalicylic acid in commercial Aspirin tablets available in the Iraqi market

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ABSTRACT

Assay of acetylsalicylic acid(ASA) utilizing some brands of Aspirin tablets available in Iraqi pharmacies by using direct acid-base titration method and spectrophotometric method for the aim of evaluation of the stability of the active ingredient in their actual environment. Direct acid-base titration method was once used to discover the concentration of active components in aspirin samples then evaluate the result with the percentage of labeling as a reference value. Although the Spectrophotometry approach showed extra correct result than direct acid-base titration when it was once in contrast to the reference value of percentage of labeling due to the excessive fee of accuracy and precision of this method, however direct acid-base titration approach shows no significant difference than the data of spectrophotometer (p-value > 0.05). Both data obtained from spectrophotometry technique and direct acid-base titration assay provide a simple, rapid, cheap, and applicable method for assay of acetylsalicylic acid concentration with a high stage of accuracy.

Keywords: ASA, Direct acid-base titration method, Spectrophotometer, Percentage of labeling, Spectrophotometric method

Introduction

Acetylsalicylic acid (ASA) the active ingredient of aspirin tablets, is a white crystalline, substance, with good stability in dry conditions but rapidly decomposes in a humid atmosphere [1]. Aspirin is now known for over a century for its analgesic, anti-inflammatory, and antipyretic action. Although these actions were superseded by other newer non-steroidal anti-inflammatory agents, aspirin still has widespread use as an antiplatelet agent to prevent the formation of thrombi [2, 3].

Analysis of the active pharmaceutical ingredients by different methods was a fundamental part of the quality control measures required to ensure both amounts and stability of the active compounds until the product reaches its expiry date, in addition to the ability of these methods to distinguish between the active compound and its degradation products [4].

Stability testing is one of the fundamental routinely performed tests utilized by pharmaceutical manufacturers to ensure the ability of the active pharmaceutical ingredients (API) to withstand the different environmental conditions before being consumed by the end-users [5, 6]. Prediction of the shelf life and the optimum storage conditions in addition to the insurance of the API quality are the results of the stability testing [7].

The spectrophotometric method has been used previously by some researchers for the determination of acetylsalicylic acid in aspirin tablets, the results showed that this method is quite accurate and no evidence of impurities interference was detected during the application of the method [8, 9]. In comparison to the other methods used for the quantitative analysis of the ASA spectrophotometric method show simplicity in sample preparation and easiness of accessibility in addition to the low cost of the entire analysis operation [10].

The aim of this study focuses on quantitative analysis of acetylsalicylic acid (ASA) and to evaluate the stability of the active ingredient of aspirin tablet that is currently available in

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the local market in Mosul city. this study will be performed by both direct titration technique as well as spectrophotometric method and the result will be compared to the percentage of labeling.

Materials and Methods

Materials

Potassium hydrogen phthalate (KHP), sodium hydroxide (NaOH), and ethanol (Scharlau S.L, Barcelona-Spain). Acetonitrile (lab.tech chemicals), acetylsalicylic acid (ASA) (central drug house(p)Ltd, India) , phenolphthalein indicator (Sigma-Aldrich , England). Aspirin tablets were collected from Mosul local markets.

Instruments

The spectrophotometer that was used for the analysis of samples was a double beam UV-visible spectrophotometer, labomed Inc., USA. The sonicated water bath used to facilitate the dissolution of aspirin tablets was DAIHAN lab tech co. LTD, Korea.

Direct titration method

The titration (acid-base titration) was done with NaOH solution which was standardized by titration with KHP solution [11], the balanced chemical equation for the reaction is shown below:

$$KHC_8H_4O_4\ (Aq.) + NaOH\ (Aq.) \longrightarrow H_2O\ (L) + NaKC_8H_4O_4\ (Aq.) \quad (1)$$

Acetylsalicylic acid was dissolved in 50% ethanol solvent [12]. The solutions of Aspirin tablets were prepared freshly by weighing and dissolving three tablets of Aspirin in 50mL ethanol (50%). Then, 3 drops of phenyl phthalate indicator were added and titrated by classical direct titration method with endpoint detected by pink color [12]. Repeating the titrations three times for each sample and calculating the direct titration percentage according to the equation (the results were expressed as mean ±SD) [13]:

$$direct\ titration\ \% = \frac{ASA\ practical\ weight}{average\ tablet\ weight} * 100\% \quad (2)$$

The result from each company will compare with the percentage of labeling of the same company.

$$percentage\ of\ labeling = \frac{ASA\ labeling\ amount}{average\ tablet\ weight} * 100\% \quad (3)$$

Spectrophotometric method

Preparation of ASA stock solution.

10% solution of ASA in ACN: H_2O (10:90 v/v) was prepared to obtain a stock solution of ASA with a concentration of 100 microgram/ml, a serial dilution of ASA solution was prepared to get the following ASA solution concentrations (0.5, 1.5, 2.5, 3.5, 4.5, 5.5, 6.5, 7.5, 8.5 and 9.5µg/mL) to draw calibration graph.

Detection of the wavelength in UV-VIS. spectrophotometer for ASA.

ASA solution was scanned in the wavelength range (190 – 400 nm) [4]. Maximum absorption spectrum (λ max) was showed at wavelength 228 nm and selected for detection ASA in the different commercially available tablets **(Figure 1)**.

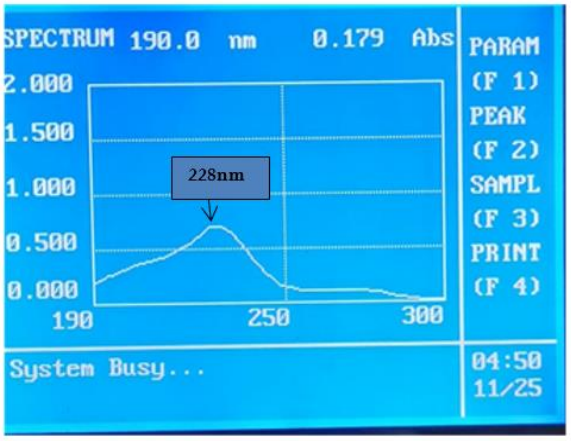

Figure 1. UV-VIS spectrum of ASA.

Preparation of calibration graph

Absorbances of all the samples were recorded at 228nm. A calibration graph was obtained by plotting the absorbance against concentration by using a computer interface, then the linear equation was obtained [14]. From the calibration curve, it was found that $R^2 = 0.9994$ and slope = 0.397 as shown in **(Figure 2)**.

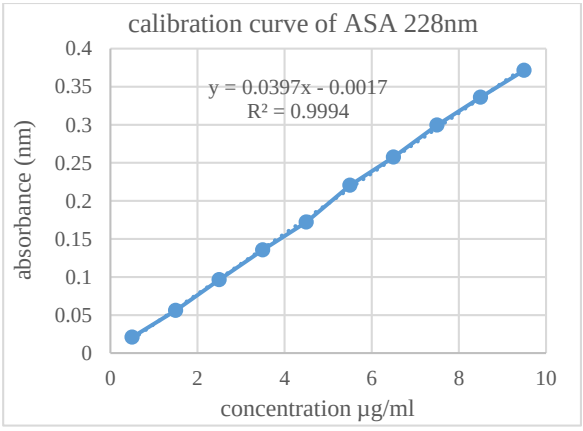

Figure 2. UV-VIS calibration graph of ASA

Assay of ASA in commercial aspirin tablets.

Accurately weight 10 tablets of aspirin grinded finely by mortar, then dissolve 10 mg of each powdered samples in up to

20 mL volumetric flask and completing the flask volume with ACN: H2O (10:90 v/v) and to achieve maximum solubility, put the resulted solution in an ultrasonic bath for 20 min. and to remove any undissolved particles filtrate the solutions through filter paper.

Prepare 10 ppm of each Aspirin sample by taking the corresponding volume according to each Aspirin tablet (dose) as shown in **(Table 1)** and measuring it with a UV spectrophotometer at 228nm wavelength.

For quantitative analysis of each measured sample use the previously drawn calibration graph and then calculating the spectrophotometric % according to the equation (the results were expressed as mean ±SD):

$$\text{Spectrophotometric \%} = \frac{ASA\ practical\ weight}{average\ tablet\ weight} * 100\% \quad (4)$$

The result from each company will compare with the percentage of labeling of the same company [13].

$$\text{percentage of labeling} = \frac{ASA\ labeling\ amount}{average\ tablet\ weight} * 100\% \quad (5)$$

Table 1. number of times dilution to obtain a concentration of 10 ppm for each aspirin sample

Sample	Weight of sample (mg)	ASA present in sample (mg)	First dilution (ml)	Concentration of solution (ppm)	Volume required for final dilution (ml)	Final dilution (ml)	Final concentration (ppm)
Company1	10	7.53	20	376.5	0.531	20	10
Company2	10	7.38	20	369	0.542	20	10
Company3	10	5.69	20	284.5	0.703	20	10
Company4	10	3.71	20	185.5	1.078	20	10
Company5	10	5.89	20	294.5	0.679	20	10
Company6	10	4.05	20	202.5	0.988	20	10
Company7	10	4.61	20	230.5	0.868	20	10
Company8	10	4.95	20	247.5	0.808	20	10

Results and Discussion

The data generated from the direct titration assay presented in **Table 2** show the differences from the percentage of labeling value of the tested samples.

Table 2. ASA analysis data obtained from direct titration assay

Sample	ASA weight labeling (mg)	Average Tablet weight (mg) (mean ±SD)*	Percentage of labeling	% direct titration (mean ±SD)*
Company1	100	130±0.33	76.92	71.48±1.59
Company2	100	137±0.10	72.99	72.95±0.81
Company3	100	169±0.28	59.17	58.82±1.40
Company4	75	201±0.16	37.31	42.97±0.29
Company5	100	167±0.44	59.88	59.2±1.00
Company6	81	196±0.25	41.33	42.3±0.87
Company7	75	158±0.21	47.47	47.26±1.32
Company8	75	146*0.39	51.37	54.13±1.32

*n=3 , SD = standard deviation.

analyzing the sample number two, five, and seven (72.95, 59.2, and 47.26 respectively) show very close value to the percentage of labeling information (72.99, 59.88, and 47.47 respectively) while the rest of the samples show either low aspirin content like in sample one (71.48) to percent labeling records (76.92), or higher aspirin content, sample four, six and eight (42.97, 42.3 and 54.13 respectively) to percentage labeling data (37.31, 41.33 and 51.37 respectively).

The data generated from the spectrophotometer assay presented in **Table 3** show the differences from the percentage of labeling value of the tested samples.

Table 3. ASA analysis data obtained from spectrophotometer assay

Sample	aspirin weight labeling (mg)	Average Tablet weight (mg) (mean ±SD)**	Percentage of labeling	% spectrophotometer (mean ±SD)**
Company1	100	130±0.33	76.92	73.71±0.087
Company2	100	137±0.10	72.99	71.95±0.075
Company3	100	169±0.28	59.17	58.2±0.035
Company4	75	201±0.16	37.31	38.91±0.042

Company5	100	167±0.44	59.88	59.65±0.035
Company6	81	196±0.25	41.33	41.05±0.015
Company7	75	158±0.21	47.47	47.57±0.015
Company8	75	146±0.39	51.37	52.65±0.01

**n=3 , SD = standard deviation.

The result from the UV-VIS spectrophotometer shows a very close value to the percentage of labeling in all tested samples.

Comparing the results obtained from direct titration assay with the data from spectrophotometric assay by using the ANOVA t-test, a nonsignificant difference ($p>0.05$) was observed indicating the possibilities of using both methods for the assay of aspirin in its dosage forms. However, the results from the spectrophotometric assay were shown to be more logically accurate because of the more sensitivity of the spectrophotometric method to the amount of acetylsalicylic acid in contrast to the direct titration method which may have some interference with the compounds that resulted from the hydrolysis of the active ingredient since the direct titration assay depends on the acid-base reaction and two of the hydrolytic products of aspirin are acid in nature (salicylic acid and acetic acid).

Aspirin was very susceptible to hydrolysis in presence of moisture with the resultant degradation products being salicylic acid and acetic acid. The restriction of salicylic acid content cloth in aspirin drugs is 3% [15]. Poor stability of aspirin in commercial pills might be due to humid conditions of improper storage or the incompatible excipients present in the tablet itself that could provide the required moisture for hydrolysis reaction [16]. Accelerated stability testing guideline for active pharmaceutical ingredients and final pharmaceutical products by WHO, designed to mimic the climate conditions of the end-user vicinity. The accelerated stability checking out is designed to verify that no modifications have been befallen in the system and /or manufacturing gadget that can adversely have an effect on the steadiness of the product and to figure out shelf life and storage conditions. However, the steadiness of achieved pharmaceutical merchandise has to be correctly monitored following a non-stop program. The motive of the ongoing stability program is to monitor the product over it is the shelf life and to determine that the product remains within specification below the storage conditions on the label [7]. HPLC [17], spectrometry [10], and acid-base titration [13] are frequent efficient techniques used in drug analysis and stability monitoring during shelf life.

For aspirin steadiness monitoring in dosage form, UV-spectrophotometer has been located to be gone well with for the intent as it is notable to precisely measure over a giant concentration vary with immoderate accuracy and precision [18]. However, with the introduction of poly component methods, UV spectrophotometry validated a great prevalent standard performance in the quantitation of compounds in combos barring the previous separation. This trouble posted the best gain over HPLC methods, such as limit cost, an awful lot of a lot of lots much less time of assessment, and minimal organic solvent lost [18, 19]. Moreover, these techniques were statistically compared to chromatographic data suggesting possible interchangeability between UV spectrophotometric techniques and HPLC for ongoing stability study of finished pharmaceutical products [20, 21].

From the obtained results we conclude that there are different variations in company content probably due to many manufacturing and storage factors.

Despite variation between values of ASA in commercially available tablets, they are considered in the quality control acceptable range reference [10].

Although the spectrophotometric technique is more accurate and easy to use in analysis than the acid-base titration method [13], the data from the acid-base titration method show no significant difference from the data of the spectrophotometer. Therefore, it can be used to confirm the results of the spectrophotometer and both techniques show close results to each other and with the acceptable range, so it can be used as an alternative to HPLC [22].

Conclusion

Both data obtained from spectrophotometry technique and direct titration assay provide a simple, rapid, cheap, and applicable method for assay of ASA concentration with a high stage of accuracy.

The result data shows stable active ingredients in aspirin tablets which ensure a good handling practice and storage conditions in local drug stores.

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