Spectrophotometric method validation studies of Aspirin

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Abstract- The validation technique was significant in retaining the quality of the final output. We can understand the terms specificity, sensitivity, accuracy, and specific detection and quantification limits. Principle component of validation is the component of quality assurance and control. Aspirin is a salicylic drug that also functions as an anti-pyretic and an anti-inflammatory. Aspirin was used against platelet assemblage and prevent arterial and venous thrombosis. There are other analysis methods, but we prefer UV-VIS spectroscopy. The procedure of forming tablets has gone through countless studies. A rapid, sensitive, and precise UV-Vis technique was developed and validated for the quick evaluation of Aspirin. The detection, linearity, accuracy, precision, and quantification limits of the approach were all verified. The optimum circumstance for testing the medication was acknowledged. The longest desirable wavelength (max) of aspirin was detected to be 226 nm. Aspirin linear equations were detected to be y = 0.004x-0.9969 r2. Validation was performed on basis of ICH requirements for specific accuracy, linearity, precision, LOQ, and LOD. According to the performance characteristics, the proposed technique was detected to be accurate, precise, and rapid for deciding Aspirin for routine survey

Index Terms- Aspirin, UV-VIS spectroscopy, and process validation are all keyword.

1. Introduction

Pain relievers are chemically known as acetylsalicylic acid. Acetylsalicylic acid (ASA) has antipyretic and anti-inflammatory properties. Pain relievers limit platelet aggregation and are also used to prevent myocardial infection and blood stroke. Painkillers are the most often used medicine worldwide, with over 26000 clinical and scientific brief articles published on the subject. (Omar, Boix, & Ulberth, 2020). In 20th century using natural and herbal ingredients for producing number of well-known drugs.

The significance and potential benefits of willow trees have been commented upon by the Assyrians in 4000 BC and the Sumerians in 3500 BC. (Fuster & Sweeny, 2011).

Joseph Buchner, a professor at Munich University, made the first discovery in the race to synthesise and pinpoint the active chemical in willow. Salicin extraction was perfected by a French chemist in 1929. Raffaele Piria produced a powerful chemical from isolated crystals of willow bark in 1839, which he termed salicylic acid (J. G. Mahdi, 2010).

Bayer began selling aspirin containing acetyl salicylic acid in 1899. The word "aspirin" comes from the combination of

the plant genus spirea and the chemical acetyl. Aspirin became a stamped tablet after being registered on February 1st, 1899. It was deemed the most popular painkiller in the world in 1950 by Guinness Book of Records. 80 million doses of aspirin are consumed daily in America, where 40,000 tonnes of aspirin are produced annually.(2006) (J. Mahdi, Mahdi, Mahdi, & Bowen) (J. Mahdi, Mahdi, Mahdi, & Bowen).

dissolve for disintegration test at appropriate amount for assesses.

2. RESEARCH METHODOLOGY

By using spectrophotometric approach for the analytical methodology as well as development, optimization and validation for aspirin is the goal of this research work and study. The mathematical calculation of maximum wave length is the true basis of work step. This research was originated in the Department of Chemistry's chemistry laboratory on the Riphah International University Faisalabad campus in Punjab, Pakistan.

2.1 Chemicals and Apparatus

Aspirin was chosen as a therapeutic agent in this research work to assess its effectiveness and quality. The selection of this is due to its medical importance as drug's ant clotting and anti-platelet Aggregation properties(Uddin, Mamun, Rashid, & Asaduzzaman, 2016). The UV Visible Spectrophotometer was the tool implement for this research work. UV-Vis spectrophotometry is approach used in laboratories to measure how much light is absorbed beyond the ultraviolet and visible spectrums. The incident light and sample typically interacts with each other it will reflect, transferred as well as absorbed.

2.1.1 Solubility studies

Various solvents, such as pure water, hydrochloric acid, sodium hydroxide, acetone, methanol, and ethanol, were used to carry out the solubility investigations test. Suited solvent is selected for aspirin validation is reveled through this study. A 10ml beaker fill up with freshly distill water and a little quantity of the medicine in powder form is used for the test of solubility. The solution is then quickly shaken continuously while being visually inspected. Medication has not been fully dissolved by distil water even if there is small quantity of particles of solute remain undisclosed in the solution

For selecting the proper solvent, repeat this method by using different sort of the solvent (Knopp et al., 2015).

2.1.2 Standard solution preparation

The standard solution was obtained by combining 50mg aspirin with 50mL of alcohol methanol to produce1000 ml.

2.1.3 Sample solution preparation

20 aspirin tablets were got at the nearby market. All of the taken tablets were broken up and were ground into powder. The powdered aspirin tablet, which weighed 50 mg, was droped into a 50 ml flask, with labeled methanol, and ultrasonicated for about 15 minutes. By using filter paper to transfer the Solution from the flask into the beaker once the distillation process is finished. The sample

solution is generated by taking 2 ml of the filtrate solution and moved it to a 25ml flask.

2.2 Experiment

- Twenty pills were weighed carefully one by one.
- After weighted them, isolate the pills from the Plagril which is the mixture of aspirin and clopidogrel.
- After separation, these tablets again weight difference.
- By mean of a pestle and mortar to crush the tablets and ground into a fine powder.
- The powder form material is ready for experiment performance after conversion.
- Weight of the sample's and the reference standard must be known.
- The known weighted sample was transferred into a flask of 50ml that had been labeled with methanol.
- Solution is ultrasonicated for 10 min.
- Distillation can begin once this vortex conjunction.
- Man filter paper 42 is used to filter the solution as well as pipette into the beaker from the flask.
- Pour 2 ml of the solution into a 25ml flask.

2.2.1 Determination of λ_{max}

The cuvette is used in which filtered solution is added. The cuvette is a tiny rectangular that used in combination .with a spectrophotometer to measure the absorbance of various wavelengths. The lambda max from aspirin was determined after sample was scanned by using UV region. (Ferree & Shannon, 2001).

2.3 Process validation of tablets

These are the critical factors considered alongside the tablet validation method:

2.3.1 Drying and sizing

The dispensing chamber was clean and that a line check was conducted in accordance with standard operating procedure (SOP).Verify that the balance was not in need of calibration. Look for a balance error of zer . Verify if the product's expiration date is later than the batch's expiration date. Verify that all items have been distributed in accordance with the(BPR) Batch Processing Report (Rudolph & Sepelyak, 2003).

Ingredient added mix well in vessel.Place the remaining ingredients in the mixer and blend on low speed for 5 minutes. Gather samples at 20,25 and 30 minutes from 6 different locations and check for content consistency. Add the granulating solution, and then gradually homogenize for 10 minutes. Examine the Wet Granules' Drying Loss (Verma, Nautiyal, Kumar, & Kant, 2014).

Table 2.1: *Milling control settings*

Variables	Responses
Size of screen Feeding rate The milling speed	Particle size distribution Loose/ tapped densities

2.3.2 Blending and Compression

Report the pre- and post-mixing before the final mixing through batch process during the 30 minutes following the last addition of the lubricant solution. Sample is collected at regular interval after every 5

minutes at 20 minutes, 25 minutes, and 30 minutes from top, middle, and bottom. Produce a composite, and then utilize it for testing. Then remaining lubricant is added, and then is agitated for 20 minutes. At intervals of 20, 25, and 30 minutes, samples are gathered from the top, middle, bottom, and composite, and they are then evaluated for testing as well as content uniformity. The finished blend is verified and weighted.(Wazade, Walde, & Ittadwar, 2012).

2.3.3 Coating and blistering

Verify the cleanliness of the coating pan and other equipment. Verify that the tablets have been subtracted, temperature of the coating solution, spray rate, spray type, and the speed of the coating pan's inlet and exhaust air. Following coating, samples were gathered for weight variation and dissolving tests (Mohammad et al., 2016).

Check and note the temperature of the air passing over the heating and sealing rollers. Verify and note whether there are additional printing instructions on labels and cartons. Make that the price overprinted on the label and carton matches the price listed in the most recent pricing list. Check the accuracy of the boxes containing the tablets after confirming accurate labeling (Snee, 2010).

2.4 Parameters

Development of ananlytical procedure and optimum validation carried out using ICH guidelines.(Sawant, Akhtar, & Master, 2013)

- System compatibility
- Selectivity/specificity
- Precision
- Linearity
- Sensitivity
- Detection limit
- Quantification limits
- Toughness/ ruggedness
- Robustness

2.4.1 System compatibility

Compatibility of the system checked before and during unknown analysis referred to system suitability. System adaptability parameters are regression logic equation, %RSD, SD, LOD, Slope, and LOD. (Jenke, 1996; Wahlich & Carr, 1990).

2.4.2 Selectivity

In comparison to selectivity, specificity is distinctive reaction which provides response to a specific analyte found in the sample, which may apply to a many kind of the analytes having similar physical and chemical properties. (Broadhurst et al., 2018).

One of the well known analytical technique is selectivity often target single analyte. Interfering species include degradation waste products, other matrix components and pollutants, shouldn't influence selectivity. The strategy decides to meet the standards of selectivity in the presence of purposely added interferents that are probably sample being studied.(Briscoe, Stiles, & Hage, 2007).

2.4.3 Linearity

According to the definition of "linearity is one of the analytical process that can produce test results that are generally related to the concentration of the sample that has specific range. Linearity refers to the ability of analytical techniques to produce results that are proportionate to the analytical range of concentration. (Chinnaiyan, Thampi, Kumar, & Balachandran, 2019).

2.4.4 Precision

Precision is defined as one type of sample give similarity of measurements under identical circumstances. It involve almost five replicate must done for the sample determinations. Precision measures how well set of measurements from different sources agree with one another are taken.

(C. Patel, Desai, & Seth, 2015).

2.4.5 Accuracy

Accuracy is a procedure which demonstrates closeness of the actual value and the average analytical value approach the other values. Accuracy method can be determined by using same problem of various solutions. Through traditional addition recovering approach duloxetine amount was calculated after recovering. (Shabir, 2005).

2.4.6 Limit of detection:

The lowest amount of analytical in an experiment that can be quantitatively quantified is always the limit of quantification of the analytical method.

Standard relative deviation is LOD = 3.3.

S = analyte's calibration curve slope (Armbruster & Pry, 2008).

2.4.7 Limit of quantification:

The limit of quantitation of an analytical process is the minimal magnitude of analysis in the sample that can be quantitatively quantified with sufficient precision and accuracy. (Shrivastava & Gupta, 2011)

The Quantitation Limit (LOQ) express as:

LOQ = 10 σ /S

σ = Relative standard deviation is denoted by (RSD)

S= analyte's calibration curve slope (Ozkan, 2018).

2.4.8 Robustness

During experiment; two different UV spectrophotometers used the UV-228 and Shimadzu UV-229. The outcome express as mean(average), standard deviation, and % RSD. (Vander Heyden et al., 1999; Wiggins, 1991).

2.4.9 Ruggedness

Slight purposeful change in the procedure setting does not affect the analytical process. It can be performed under normal conditions. Level of ruggedness determined under the repetition of situations.

3. RESULTS and DISCUSSION

3.1 Results of solubility studies

Different solvents such as distill water, Methanol, acetone, ethanol, HCl, NaOH employed for checking the aspirin solution .The results are as follow;

Table 3.1: *Solubility results of Aspirin*

Solvent	Aspirin
Distilled water	Sparingly soluble
0.1 N HCl	Sparingly soluble
0.1 N NaOH	Sparingly soluble
Acetone	Insoluble
Methanol	Freely soluble
Ethanol	Freely soluble

3.2 ƛ max determination

Standard Solution of aspirin transfer into 10ml beaker mark up with methanol absorbance of Solution was measured in the rage of (200-400nm). The absorption spectrum shown at wavelength λ max is 226nm.

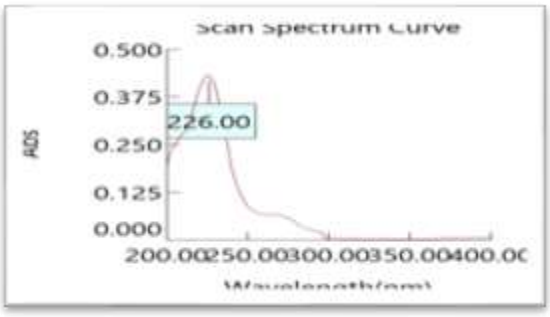

Figure 3. 1: *UV spectrum of aspirin*

3.3 Description of the process

3.2.1 Dry mixing

The initial stage of dry mixing was mathematically mixing which was followed by the final mixing .For mixing the Mechanical Sifter ID PR.TBM.EQ.121 was usedFor Geometrical Mixing the Mechanical Sifter ID PR.TBM.EQ.121 was used.

Table 3.2:*Sampling plan*

Batch No.	Testing Parameter	Place	Time	Quantity	Number of Samples	Instrument of Sampling
123	Assay	Top, Mid	20 ,25	4.5 g each	03 x 03*	Sampling
124	Assay	Top, Mid	20, 25	4.5 g each	03 x 03*	Sampling
125	Assay	Top, Mid &	20, 25 &	4.5 g each	03 x 03*	Sampling Lanc

Three samples were taken top, middle, and bottom. Time for final mixing is 20, 25, and 30 minutes. Table 3.2 shows the Sampling plane in dry mixing, which describes the location, time, quantity of samples, apparatus, and testing variables.

Table 3.3: *Parameters for testing*

30 Minutes selected for final mixing on

Batch No									
	Parameters							Equipment Parameters	
								Velocity	Time interval
123	Place	20 min.	25 min.	30 min.	20 min.	25 min.	30 min.	8rpm	20min., 25min., 30min.
	Top	100.79	98.88	106.13	101.18	98.64	99.77		
	Mid	103.15	100..95	99.91	99.81	99.10	100.65		
	Bottom	104.67	104.23	100.59	98.18	101.05	96.87		
	Mean	102.87	101.555	102.21	99.72333	99.59667	99.0966		
	STD	1.95509	3.78302	3.411803	1.501877	1.279466	1.97791		
	CV	0.024	0.037	0.033	0.015	0.012	0.019		
124	Place	20 min.	25 min.	30 min.	20 min.	25 min.	30 min.	8rpm	20min., 25min., 30min.
	Top	98.96	99.40	101.17	96.41	96.59	98.23		
	Mid	97.35	96.80	99.93	93.75	91.41	92.24		
	Bottom	98.14	98.17	100.74	91.76	96.36	101.24		
	Mean	98.15	98.12	100.61	93.97	94.78	97.23		
	CV	0.0082	0.01325	0.00625	0.02483	0.03087	0.0471		
	STD	0.805	1.300	0.629	2.333	2.9365	4.581		
125	Place	20 min.	25 min.	30 min.	20 min.	25 min.	30 min.	8rpm	20min., 25min., 30min.
	Top	100.59	101.43	101.78	96.87	93.18	94.58		
	Mid	103.68	104.52	101.80	98.35	99.18	94.54		
	Bottom	101.73	101.05	102.54	95.97	93.62	91.73		
	Mean	102	102.33	102.04	97.063	95.326	93.616		
	STD	1.56259	1.90321	0.433128	1.201721	3.344329	1.63402		
	CV	0.01532	0.01859	0.004245	0.012381	0.035083	0.01745		

the

3.3Process Capability

Final result of process capability is indicated in the table 4.11

Table 3.4: *Final result of process capability*

Parameters		B.123	B.124	B.125	USL	LSL	CP	Results
Assay of Grains (%)	IPC	101.54	101.91	102.01	110	90	13.46	Too much capable
	Aspirin	98.1	95.9	93.58	115	85	2.21	Too much capable
Weight Variation(mg)		550.5	550	552.4	558.25	541.75	2.17	Too much capable
Friability (%)		0.19	0.19	0.2	0.5	---	14.43	Too much capable
Hardness (N)		103.8	112.7	106.3	170	20	5.45	Too much capable
Thickness (mm)		4.9	4.9	4.85	5.00	4.5	2.89	Too much capable

3.5 Validation results

3.5.1 Linearity

Appropriate painkiller dosage that performed as expected sample option were added to volumetric flasks of 10ml about 6 in numbers. In order to achieve final concentration flask are roughly diluted with and the concentration which is achieved is 5, 10, 15, 20, 25, and 30 ml/l. calibration curve were computed and equation for drug regression through plotting between absorbance versus concentration. (Gupta, Sharma, Pandotra, Jaglan, & Gupta, 2012).

Table 3.6: *UV-VIS spectrophotometric Asprin procedure calibration data table*

Concentration	1st Linerity Absorbance	2nd Linerity Absorbance	3rd Linerity Absorbance	Mean/average
5	0.216	0.217	0.219	0.2173

				33
10	0.218	0.219	0.221	0.219333
15	0.22	0.222	0.222	0.221333
20	0.222	0.225	0.224	0.223667
25	0.224	0.226	0.225	0.225
30	0.227	0.228	0.227	0.227333

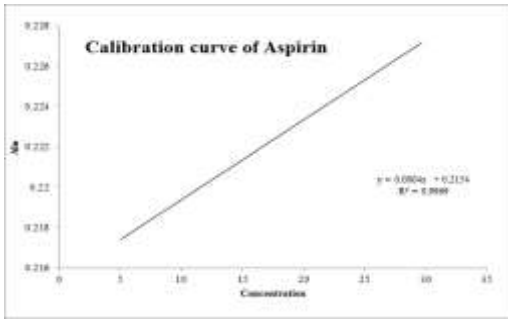

Figure 4.2: *plotted a graph using x axis-concentration and y axis-average absorbance give calibration curve*

3.5.2 Precision:

Five replication performed by the standard solution to evaluate the accuracy of the analytical process. In addition SD and RSD were acquired together, along with table of eavesdrop. The RSD value was less than 2, describes that the active process is competent(Alsmeyer et al., 2016).

Table 3.7 : *Precision study*

Taken concentration	Found concentration	Recovery	Mean	SD	RSD
17.5	17.02	98.351	17.26	0.33941255	1.9664615
35.1	35	99.156	35.05	0.07071068	0.2017423006
44.125	44.74	99.722	44.435	0.43487067	0.97872204
54.15	54.17	100.6	54.16	0.01414213 6	0.02611177 2
71.2	71.93	99.62	71.565	0.51618795	0.72128547 5

3.5.3 Accuracy

This procedure involved double-checked the samples. Table 4.13 describes the findings of the study.The data reveals that RSD is lesser than 2, and restoration rates are 98.51%, 99.93%, and 99.96%.

Table 3.8:*aspirin accuracy measurements*

Level of recovery	Amount utilized	Amount recovered	Recovery	SD	RSD
50	5.2	4.947	98.24	0.258106	0.0520301
	5.4	4.964	98.95		
	5.6	4.971	98.35		

Average	5.4	4.960667	98.51333333		
100	10.1	9.91	99.91	0.279529	0.0281122
	10.3	9.97	99.98		
	10.7	9.95	99.92		
Average	10.36667	9.944333	99.93666667		
120	15.6	14.85	99	0.3592245	0.0240466
	15.7	14.99	99.99		
	15.5	14.98	98		
Average	15.6	14.94	98.99666667		

3.5.4 LOD detection of limit

ICH and FAD guidelines are used for computing LOD data. calculate the detection limit through formula;

LOD = 3.3σ/S

Relative standard deviation is determined using equation

S = analyte's calibration curve slope

Table 3.9:*Calculating LOD data*

Sr. No	Concentration	Absorbance
1	5	0.216
2	10	0.218
3	15	0.22
4	20	0.222
5	25	0.224
6	30	0.227
	Average	8.860583333
	SD	0.004020779
	Slope	0.0004

Put the calculated values of slop as well as standard deviation into equation no. 4.1from the data table.

LOD= 3.3 *standard deviation/ calibration slope

=3.3* 0.0004/0.00402079

= 0.328

3.5.5 LOQ limit of quantification

LOQ is calculated on the base of ICH guanidine the limit of quantification is determined from this formula;

LOQ=10 σ /S. Equation no. 3.2

σ = Relative standard deviation (RSD)

S = slope calibration curve of the analyte

LOQ = 10 * SD/Slope calibration curve Eequation no 3.2

Put the value of stander deviation (SD) and calibration curve value from given data table in to equation no 4.2

= 10*0.0004/0.00402079

LOQ = 0.995

3.5.6 Robustness

Wavelength variation was noticed to test the adjustment of method. For each phase, five samples of solution were created at 100% concentration. The relative standard values convey details about the procedure. The low RSD number indicates that this process was successful.(Kazi, Shariare, Al-bgomi, Hussain, & Alanazi, 2018).

Table 3.10: Data on the UV-Vis spectrophotometric method's robustness based on a change in wavelength of 229 nm

Sr.No	Concentration	Absorbance	Calculated amount
1	30	0.217	30.08
2	30	0.219	30.2
3	30	0.221	30.6
4	30	0.223	30.7
5	30	0.225	30.8
		Mean	30.476
		SD	0.317616
		%RSD	1.0422

3.5.7 Ruggedness

Six samples with a concentration of 30 ml were generated for testing ruggedness, and UV-visible spectrophotometer is used for checking of absorbance. Table 3.11 shows the experiments results.

Table 3.12: *toughness testing for analyst 1 & 2*

Analyst 1			Analyst 2		
Concentration	Absorbance	Calculated amount	Concentration	Absorbance	Calculated amount
30	0.216	30.13	30	0.217	29.16
30	0.218	30.05	30	0.219	29.909
30	0.220	29.890	30	0.221	29.036
30	0.222	29.805	30	0.223	30.15
30	0.224	29.781	30	0.225	30.17
30	0.226	29.954	30	0.227	30.05
	Mean	29.935		Mean	29.74583
	SD	0.137297		SD	0.511756
	RSD	0.004586		RSD	0.017204
	%RSD	0.45865		%RSD	1.7204

Conclusion

For the dissection of Paracetamol in its tablet making, a unique, secure, and

delicate process of spectrophotometric quantification has been devised in the UV-region. Methanol was used as the diluent in the method's development and validation for the analysis of aspirin. These methods of development and validation do not intrude with spectrophotometric estimates. All of the analysis's parameters were selected on the basis of ICH guidelines and statistically authorized handling RSD and%RSD.

Maximum wavelength (max) of aspirin was discovered is 226 nm and results were explained in 4th chapter. Aspirin was shown to be linear throughout the concentration series of 5–30.Drug regression equation was calculated by plotting absorbance vs. concentration calibration curve. It was determined that the linear equations were found to have y = 0.0004x 0.2154 with the correlation coefficient r2 is 0.09969. Determining parameters like Precision, Accuracy, LoD, LoQ, Ruggedness, and Ruggedness results revealed that the system was suitable. Information about the appropriateness of system was indicated using relative standard deviation (RSD). The fact that RSD was less than 2 demonstrates that the process was viable of operating.

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