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TO DEVELOP VALIDATED METHOD OF SALICYLIC ACID BY UV-VISIBLE SPECTROSCOPY AS IMPURITY IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

A method to form a UV-Visible active derivative of Salicylic acid was developed. The method was based on the reaction of salicylic acid, forming a colored derivative, which was UV-Visible active. The method was used to analyze pharmaceutical dosage form for trace amount of salicylic acid using UV-Visible spectrophotometer. The formed derivative exhibits maximum absorbance at λ_{max}= 505nm. The method was validated in the range of about 10-90µg/ml.

KEYWORDS: Salicylic acid, Ferric Chloride regent, UV-Visible spectrophotometer.

1. INTRODUCTION

Salicylic acid, also called ortho- hydroxybenzoic acid, a white, crystalline solid that is chiefly in the preparation of aspirin and other pharmaceutical products.[1] Salicylic acid is a lipophilic monohydroxybenzoic acid, a type of phenolic acid, and a beta hydroxy acid (BHA). It has the formula $C_7H_6O_3$.[2-3] In addition to serving as an important active metabolite of aspirin (*acetylsalicylic acid*), which acts in part as a prodrug to salicylic acid, it is probably best known for its use as a key ingredient in topical anti-acne products.[4]

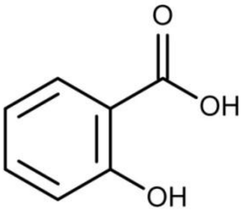

Fig. 1: Structure of Salicylic acid.

Salicylic acid produces its anti-inflammatory effects via suppressing the activity of cyclooxygenase (COX), an enzyme that is responsible for the production of pro-inflammatory mediators such as the prostaglandins. In low concentration salicylic acid has keratoplastic activity, and in higher ones, it has keratolytic activity.[5]

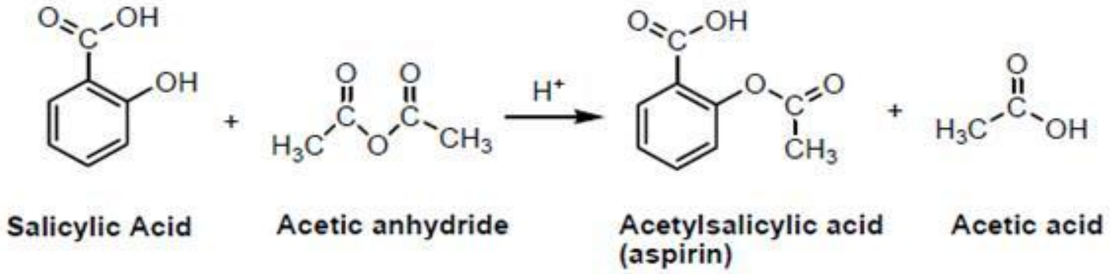

Fig 2: Synthesis of Aspirin.[6]

Phenols (such as salicylic acid) react with ferric chloride to form colored (blue or violet) complexes. A very simple method of detection of the free salicylic acid in aspirin could be based on the different coordinating capacity of the salicylic derivative with the octahedral Fe^{+3} cation. Thus, the yellow FeCl3 aqueous turns dark blue in the presence of a very light quantity of free salicylic acid.[7-9]

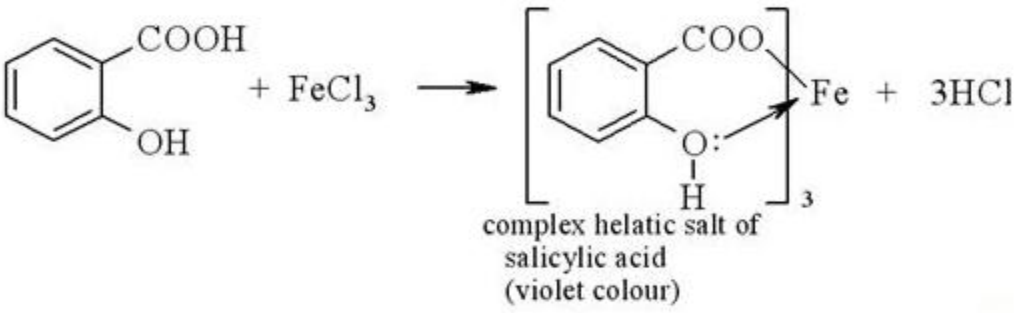

Fig 3: Formation of Salicylate ion.

2. MATERIALS AND METHODS

2.1. Apparatus: The Spectrophotometric measurements were carried out using Agilent UV-Visible Spectrophotometer with 1cm quartz cell.

2.2. Materials

All chemicals used were of analytical reagent grade. Distilled water was used to prepare solutions wherever required. Ferric chloride, hydrochloric acid, salicylic acid pure sample and tablets of brand namely Ecosprin- 75mg were purchased from local commercial sources.

2.3. Reagents

Hydrochloric acid (1%) was prepared by appropriate dilution of concentrated acid with water. A 1% solution of Ferric chloride was prepared by dissolving suitable amount of the commercially available reagent to 100 ml with 1% of HCl in a volumetric flask.

2.4. Standard drug solution

Standard drug solutions of 100µg/ml was prepared using distill water. Further dilution was carried out using 1% Ferric chloride solution to obtain 10µg/ml dilution.

2.5 Procedures

2.5.1 Preparation of calibration curve

Into a series of 10 ml calibration flasks, aliquots of standard drug solution (1-9 ml of 100µg) equivalent 10-90 µg/ml were accurately transferred and 1ml of 1% Ferric chloride reagent was added to each. Further the volume was made up to the mark with distill water. The absorbance of each solution was then measured at 505 nm, against the respective solvent. In either case, calibration curve was prepared by plotting the absorbance versus concentration of drug. The concentration of the unknown was read from the respective calibration curve or computed from the regression equation derived using the Beer’s law data.

2.5.2 Analysis of tablets

Ten tablets of aspirin (Ecosprin 75mg) were weighed and crushed into a fine powder using a Pestle and Mortar. An amount of tablet powder equivalent to 200 mg of Aspirin was transferred into a 50 ml volumetric flask. The content was shaken well with about 20ml distill water for 20 min. The mixture was diluted to the mark with the same solvent. It was filtered using Whatman No 42 filter paper. Subsequent portion was diluted to get a working concentration of 100µg/ml and subjected to analysis.

3 RESULT AND DISCUSSION

3.1 Spectral characteristics

The salicylic acid solution in 1% Ferric chloride showed absorption maximum at 505nm. At this wavelength 1% Ferric chloride had insignificant absorbance. Therefore, further investigation for the analysis of salicylic acid was carried out at 505nm. Fig. 1 represents the absorption spectra of salicylic acid.

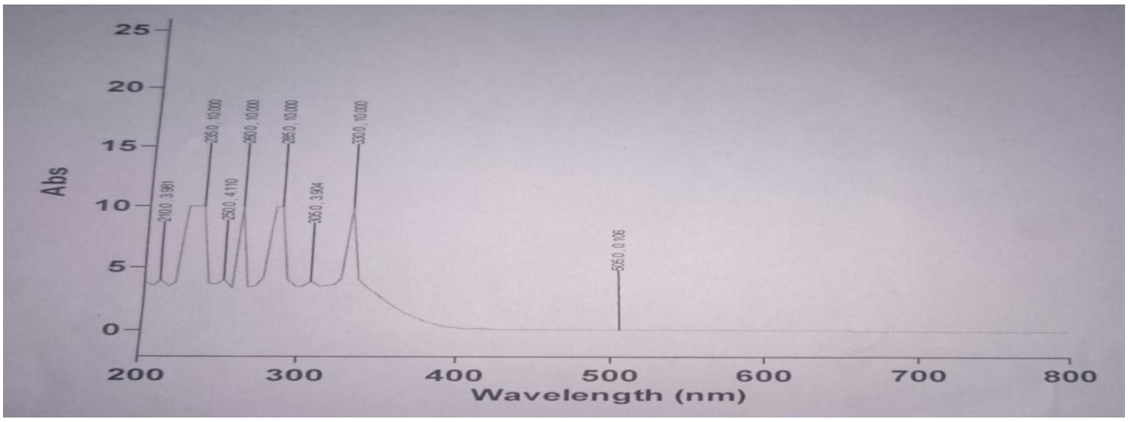

Fig 1: UV Spectrum of Salicylic Acid (λ_{max})

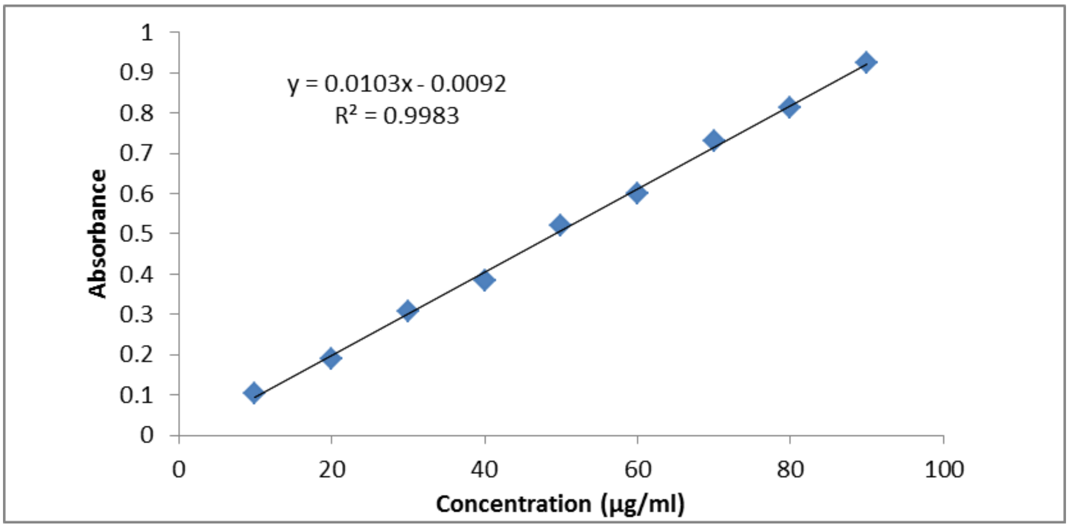

Fig 2: Calibration curve of Salicylic acid.

3.2 Method validation

3.2.1 Linearity and Range

A linear relationship was observed between absorbance and concentration in the working range of 10-90µg/ml of drug in the solution as shown in fig.2, and correlation coefficient (r) was as shown in table 1.

Table 1: Regression and Analytical Parameters.

λ max, nm	**505nm**
Beer's law limit (µg/ml)	**10-90**
Molar Absorptivity	1253.587
Sandell sensitivity	10.37×10^{-3}
Regression equation, Y	y = 0.010x – 0.009
Intercept, (a)	0.009
Slope, (b)	0.010
Corelation coefficient	0.998

3.2.2 Specificity

About 4ml of standard stock solution was pipette out in three 10ml volumetric flasks along with 1ml 1% ferric chloride reagent. The volume was made upto the mark with distill water (40µg/ml). The absorbance of these solutions was recorded. For specificity determination same concentration dilutions were made and about 1mg of excipient was added. The absorbance of these solutions was recorded. The concentration of the solution was determined and % interference calculated.

Table 2: Specificity study for Salicylic acid.

S. No.	**Conc. (µg/ml)**	**Before addition of excipients**		**After addition of excipients**		**% Interference**
		Abs.	**Conc.**	**Abs.**	**Conc.**	
1	40	0.3977	40	0.3989	39.9	-0.30
2	40	0.3992	40	0.3936	39.9	1.40
3	40	0.3944	39.9	0.3954	40	-0.25
Mean						0.85

3.2.3 Repeatability

About 4ml of standard stock solution was pipette out in three 10ml volumetric flasks along with 1ml 1% ferric chloride reagent. The volume was made upto the mark with distill water (40µg/ml). The absorbance of these solutions was recorded.

Table 3: Repeatability study for Salicylic acid.

Theoretical conc. (µg/ml	**Absorbance**	**Observed conc. (µg/ml)**	**Mean conc. (µg/ml)**	**S.D**	**%RSD**
40	0.4091	40.1	40	0.00074	0.185
40	0.3936	39.9			
40	0.4061	40			

3.2.4 Intra- day precision

3, 4, 5ml of the standard stock solution was pipette out in three 10ml volumetric flasks along with 1ml 1% ferric chloride reagent. The volume was made upto the mark with distill water resulting in solution of 30 µg/ml, 40µg/ml, 50µg/ml of drug. The absorbance of these solutions was individually were measured thrice within a day and recorded.

Table 4: Intra- day precision study for Salicylic acid.

Conc. (µg/ml)	Absorbance			Conc. Found (µg/ml)			Mean conc. (µg/ml) ±SD	%RSD
	1	2	3	1	2	3		
30	0.2990	0.2915	0.3053	30	29.9	30.1	30±0.0007	0.07781
40	0.4056	0.4050	0.4197	40	40	40.2	40.06±0.00067	0.18566
50	0.4955	0.4980	0.5189	49.9	49.9	50.1	49.96±0.00059	0.06364
Mean								0.1090

3.2.5 Inter- day precision

3, 4, 5ml of the standard stock solution was pipette out in three 10ml volumetric flasks along with 1ml 1% ferric chloride reagent. The volume was made upto the mark with distill water resulting in solution of 30 µg/ml, 40µg/ml, 50µg/ml of drug. The absorbance of these solutions was individually were measured thrice in three days and recorded.

Table 5: Inter- day precision study for Salicylic acid.

Conc. (µg/ml)	Absorbance			Conc. Found (µg/ml)			Mean conc. (µg/ml) ±SD	%RSD
	1	2	3	1	2	3		
30	0.2912	0.2995	0.3057	30	29.9	30.1	30±0.00063	0.08581
40	0.4063	0.4047	0.4200	40	40	40.2	40.06±0.0007	0.20561
50	0.4956	0.4989	**0.5181**	49.9	49.9	50.1	49.96±0.00064	0.07245
Mean								0.12129

Table 6: Result of estimation of Salicylic acid as impurity in Pharmaceutical dosage form.

S.No.	Absorbance	Dil Factor	Content (mg)	Weight Taken (mg)	Label claim (mg)	% of SA in ASA
1	0.2292	2000	252	200	75	2.82
2	0.2096	2000	252	200	75	2.58
3	0.2245	2000	252	200	75	2.76

4 CONCLUSION

The determination of salicylic acid (SA) in acetylsalicylic acid (ASA) / aspirin marketed tablet Ecosprin 75 was limited to 2.5-2.8%. Hence, the established colorimetric method is good enough to meet the requirements of the USP and IP Pharmacopoeia which demands SA content in ASA tablets of less than 3%.

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