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Spectrophotometric determination of Sodium Salicylate in pharmaceutical preparations by coupling with Diazotized Para-amino benzoic acid

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ABSTRACT

Sensitive, simple and rapid colorimetric procedure for the assay of the smaller amounts measures from sodium salicylate at pharmaceutical preparations (topical-solution) was examined. The procedure is focus on the diazotization and a reaction coupling between sodium salicylate and diazotized para-amino benzoic acid in alkaline medium for the formation of an intensive bright yellow soluble water colour which was being stable, which gives highly absorption at 452nm. The law of Beer was Introduced on the range of concentration from 2-30 $\mu g.ml^{-1}$ of sodium salicylate, the sensitivity of sandell index and the molar absorptivity were 0.0188 $\mu g/cm^2$, 8.5013×10^3 l mol^{-1} cm^{-1} subsequently, The procedure does not need to the control of temperature and the extraction by the solvent. The ideal circumstances for all increase colour are portrayed, the procedure was examined and it was given excellent application on the sodium salicylate quantitative assay at topical- solution preparations. The public excipient substances and additives did not have any influence the examined procedure.as shown in Fig.1.

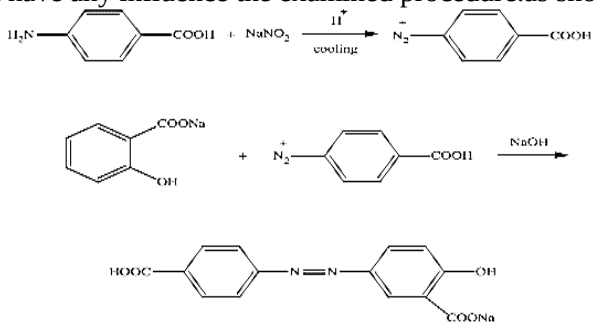

Fig.1.scheme for Colored Azo dye fromation

KEY WORDS: Diazotization coupling reaction, spectrophotometric determination, sodium salicylate, para-amino benzoic acid.

1. INTRODUCTION

Sodium salicylate is the crystalline powder and white or almost white colour, or crystals with small, colorless or flakes shiny, water freely soluble, ethanol sparingly soluble (96%). It is a sodium 2-hydroxybenzene carboxylate, $C_7H_5NaO_3$.

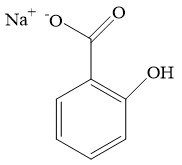

Fig.2. Structure of Sodium Salicylate

Sodium salicylate was a salt for sodium with salicylic acid. It was formed by the reaction between sodium phenolate and carbon dioxide by using higher pressure and temperature. In the literature, Where it had extracted by methyl salicylate that it was obtaining from winter green plants or from sweet birch tree that result from the bark, by adding it with surplus of consented solution (sodium hydroxide) and making reflux operation for it with heating.

The substance is utilized as therapy as an antipyretic and a pain relieving. Sodium salicylate additionally performs about as non-steroidal calming (NSAID) drug, also it affects as anti-cancer in the infected cells and otherwise necrosis. It was using as potential alternative for aspirin drug that was giving to sensitive people for this drug. Sodium salicylate was been utilized like the phosphor for the discovery of electrons and vacuum ultraviolet radiation.

In the present work, the stable diazotized para-amino benzoic acid reagent has been proposed to determine sodium salicylate in pharmaceutical preparations (topical-solution) by utilizing the (azo-coupling) reaction in basic media. The serious splendid yellow that was resulting in the product, it was computed spectrophotometrically at 452 nm. The new method for investigation was exact, rapid and simple. The procedure was making a very good application in the investigation for sodium salicylate in pharmaceutical preparations (topical solution).

2. EXPERIMENTAL

Apparatus: Every spectral estimations were executed on applied UV-Visible digital 160 recording spectrometer (double - beam) (Japan), Analytical balance (Sartorius BL 210S), pH meter, Jenway 3020, Heating-cooling water bath (Haake, Fe3).

Material and reagents: The Chemical substances that were utilized in the procedure with very high degree from purity and did not required to refining, the solutions were obtained by the next steps. Sodium salicylate (500 µg.ml-1) solution: It was supplied by dissolution for (0.05g) of sodium salicylate (SDI) in (100) mL deionized water. The solution is at that point exchanged to a dim bottle where it is steady for no less than 1 month.

Para-amino benzoic acid (3 x10-3M) (Diazotized reagent solution): It was obtained by dissolution (0.01 gm) of para-amino benzoic acid (Fluka) with highly purity in (5mL) of deionized water, after that (2 mL) of 1 M HCl (BDH) was added and shacked well, then Continued by adding of (0.009 gm) from sodium nitrite (BDH) and completely shaking, after that the volume was diluted to (25 mL) and the was cooling at temperature degree (5°C) for 30 min, The solution was taken to a dark bottle and leaved in the refrigerator that was steady for two weeks. Hydrochloric acid (BDH) (1M): It was provided by dissolution reasonable measure of conc. HCl to (100 mL) by deionized water.

Sodium hydroxide (BDH) (0.5M): It was supplied by dissolution (2.0 gm) of sodium hydroxide in the volumetric flask (100 mL), the completed volume was to the label with deionized water.

Procedure: Separately, volumetric flasks (25mL), the volumes was increasing of (500 µg.ml-1) sodium salicylate from the standard working solution were exchanged to cover a range between 2-30 µg.ml-1 in the end dissolution, 0.5M sodium hydroxide 1mL solution, 2 mL form diazotized para-amino benzoic acid solution 0.003M are added and dissolute to the lebal by deionized water. After that it was mixing very good ,then it was leaving for 15min. at 25°C, the intensive bright yellow colour for the result was gave the highly absorbance computed at 452 nm versus a blank reagent that was including each the materials without the sodium salicylate and the calibration curve was built.

Assay Procedure for salicylic acid in Pharmaceutical Preparations: A topical-solution sample 25 mL was conveyed to volumetric flasks 100 mL, then it was dissolute to the label with deionized water. An aliquot for the using solution 1mL was put in volumetric flask 25 mL, 2mL (0.003M) diazonium agent, 1mL (0.5M NaOH), that we're adding, the completed volume to the label by deionized water, put away for 15 minutes, the measured absorbance for this solution was at 452 nm. The salicylic acid concentrations was given by utilizing the calibration curve officially made and portrayed previously.

This procedure was obtained for 3 trade kinds for topical solution that are, Avomack topical solution (MECP, Riyadh-KSA, Label claim: 16.7% w/w Salicylic acid), Duofilm topical solution (ITD, Sligo, Ireland, Label claim: 16.7% w/w Salicylic acid), Nocal topical solution (Jordan, Label claim: 10% w/w Salicylic acid).

Table.1. Salicylic acid investigation in some pharmaceuticals by utilizing the suggested technique

Brand	Conc. Salicylic Acid µg. ml^{-1}		E %	Rec. %	RSD % N = 5	Conc. Sodium Salicylate µg. ml^{-1} *
	Taken	Found				
Avomack Topical solution	4	3.977	-0.575	99.425	0.679	4.609
	16	15.890	-0.687	99.313	0.930	18.416
	26	25.770	-0.884	99.116	1.300	29.867
Duofilm Topical solution	4	4.030	+0.750	100.750	0.590	4.670
	16	16.200	+1.250	101.250	1.010	18.775
	26	25.880	-0.461	99.539	0.903	29.994
NOCAL Topical solution	4	3.960	-1.000	99.000	0.499	4.712
	16	15.920	-0.500	99.500	0.841	18.451
	26	26.400	+1.538	101.538	1.410	30.597

*Every of the values that was utilizing in the table, It was relates with the quantity of Sodium salicylate, It was result from the multiply of the quantity of the salicylic acid per the sample by the conversion factor of 1.159, which was being equal to the output of dividing the molecular weight of sodium salicylate on the molecular weight of the salicylic acid.

3. RESULTS AND DISCUSSION

The perfect reaction circumstances was studied. The impacts of various information on the visual characteristics for the colour of the azo dye have been examined, the reaction circumstances are given.

Reagent volume influence: The diazonium revealer (0.003M) volumes was examined by utilizing the range between 0.1-5 mL on the absorbance intensity, it was has been studying 2 mL volume was the perfect volume.

Acid volume influence: The presence of acid that was adding in the suggested procedure resulted in an increasing on the absorbance intensity for the formed product, so thus, acids like CH_3COOH, HCl, H_2SO_4 and HNO_3 are checked up, all these acids was giving verging on equivalent intensity, therefore; HCl was chosen for the next tests and, 2 mL volume was the perfect from the chosen acid that was obtaining. Highly sensitive which it utilized in following experiments.

Base volume influence: The colour product formed was giving highly absorbance and it was making more stable and intense in basic medium, so that, the various basic solutions effect on the colored result were examined like potassium hydroxide, sodium hydroxide, sodium carbonate, sodium acetate and ammonium hydroxide. Highly sensitivity and stability were given just when the reaction was performed with the attendance of the solution of sodium hydroxide. The various concentrations of NaOH effect were examined, 0.1-4 M concentrations for the using base with concentration 0.5 M appears to be ideal. The 0.5 M NaOH volumes effect were as well examined between 0.1 to 5 Ml, 1mL volume was the perfect volume and utilizing in the next tests.

Order Addition influence: The ideal order addition that obtains the maximum absorption was (D+B+R) wherever (B=base, R=reagent and D=drug substance) that was choosing in the following tests.

Temperature influence: The produced compound from a studied procedure were examined at various temperatures. The absorbance values that obtained from the outcomes demonstrate that it was staying about consistent in the range of temperature 0-70ºC, While, the absorbance value at the increasing temperatures was Reduced, demonstrating the disintegration of the result on the heating for a long time. The stability of the colored compound was between 15 - 20ºC. So that, this range of temperature was chosen in examined procedure.

Reaction Time influence: The highly intensity of colour arrived after that the sodium salicylate was reacting instantly with the solution of reagent. It was making steady after time 15 minute. So that 15 minute evolution time was taken as the prefect in the common method of assay. The colour resulted was steady for 2 days. The practical circumstances for the investigation for sodium salicylate were instituted. The reaction Diazonium happened in the acidic medium and 1M concentration for hydrochloric acid was chosen, the absorbance for the colour compound formed has been highly stable and intense in basic medium.

Absorption spectra: The dilute solutions from sodium salicylate in under the foregoing form. The Practical circumstances, was blending with diazotized para-amino benzoic acid in Attend the sodium hydroxide, the bright yellow intense colour compound instantly established. It gives highly absorption at 452nm, at the same time the reagent solution (blank) gives no absorption at the same wavelength. Fig.2 gives the spectra of absorption. The highly absorption wavelength was at 452nm, it was yet utilized for the next determinations.

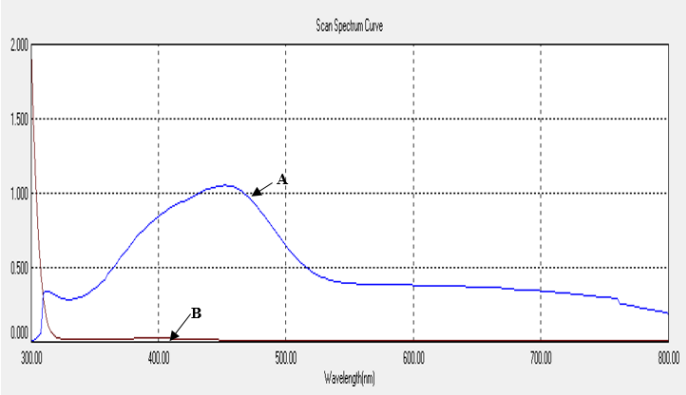

Figure.3.The spectra of absorption :

A : sodium salicylate (20 µg . ml-1) + para-amino benzoic (3x10-3) (the resulting compound) opposite the(blank) reagent. B : the reagent solution (blank) opposite D.W.

Calibration curve: By using the established practical circumstances, the linear relation between the sodium salicylate concentration with the absorbance was noted during the range of concentration 2- 30µg.ml^{-1}, Fig.3, an intercept and the correlation coefficient were 0.0821, 0.9990 Respectively. The beer's law was given negative deviation at the concentrations up to 30 µg.ml^{-1} from the sodium salicylate. The molar absorptivity was 8.5013×10^{3}l.mol^{-1}.cm^{-1}.

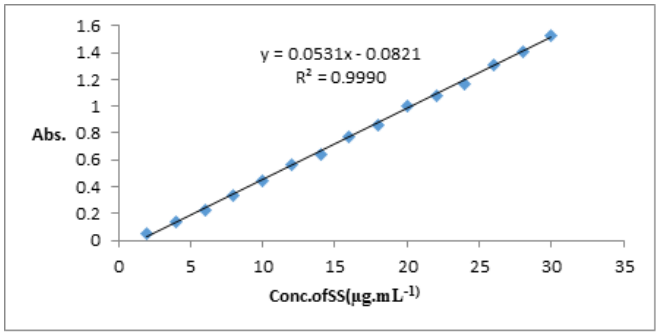

Figure.4.Calibration curve for sodium salicylate (ss)

Precision and accuracy: For investigation of a precision and an accuracy for the calibration curve, sodium salicylate was designating by utilizing a three various concentrations. The outcomes appeared at table.2 was demonstrated a good satisfying accuracy and precision.

Table.2. Precision and accuracy of examined procedure

Number	Conc. Of Sodium Salicylate 25mg/ml		Error % *	Recovery *	RSD % *
	present	found			
1	4	3.964	-0.900	99.100	0.374
2	16	16.110	+0.687	100.687	0.990
3	26	26.200	+0.769	100.769	1.200

*** Average for five investigations**

Product nature of and the mechanism of reaction: To observe the structure for the product compound (the ratio between sodium salicylate to diazotized para-amino benzoic acid) for the intense bright yellow azo colour that was resulting from reaction, mole-ratio method and Job's method of continuous variations have been utilized. The data that was resulting discover that the colour has been established by the reaction of sodium salicylate with diazotized para-amino benzoic acid with the ratio for 1:1, Fig (5&6).

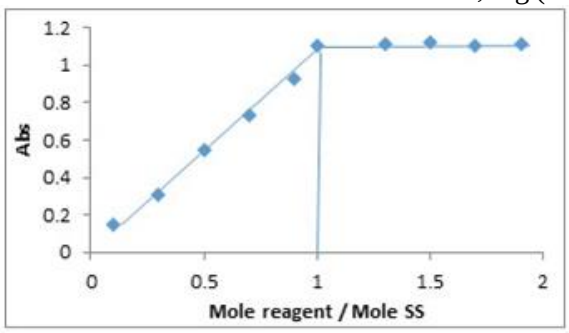

Fig.5.Mole ratio plot

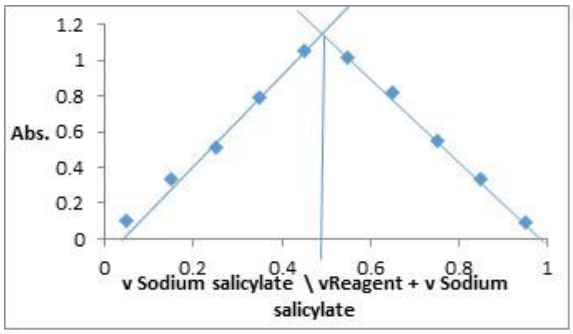

Fig.6.Continuous variation plot

The stability constant was computed for the dye of azo in the hydrous solution, by using all the circumstances of practical method, the constant was equal to 28×10^6 l.mole^{-1}. The gradient equation was given, the analytical data for this method obtained are given in Table.3.

Table.3. Analytical properties of the developed method for the investigation of sodium salicylate

Parameter	studied method
Gradient equation	Y=0.0531x- 0.0821
Linear range (µg ml^{-1})	2-30
Correlation coefficient, r^2	0.9990
Detection limit (µg ml^{-1})	0.064
Average of recovery %	99.702
Average of RSD %	0.854
Sandell's sensitivity (µg cm^{-2})	0.0188
Molar absorptivity l mol^{-1} cm^{-1}	8.5013*10^2

Interferences influence: The probably analytical enforcements were evaluated for the new suggested Procedure, the interferences effect for the excipients on the different levels for the quantitative assay of (20µg.ml^{-1}) of Salicylic acid by utilizing the studied procedure have been tested, the outcomes are obtained by table.4.

Table.4. Excipients influence on the investigation of (20µg.ml^{-1}) of Salicylic acid

Excipient	Concentration of Salicylic acid µg.ml^{-1}	E%	REC% Recovery
Talc	19.890	-0.550	99.450
Lactose	20.102	+0.510	100.510
Starch	19.800	-1.000	99.000
Mg stearate	19.790	-1.050	98.950
Poly vinyl pyrolidone (PVP)	20.220	+1.100	98.900
Benzoic acid	20.125	+0.625	100.625
Manitol	19.880	-0.600	99.400

*Average for five determinations

Application procedure: The examined procedure were checked up on the quantification of salicylic acid in topical solution preparations. Three kinds of topical solution preparations having salicylic acid were tested, there was obtaining a better precision and accuracy as appeared in Table.5. The examined procedure were given successful comparison with the standard procedure.

Table.5. Application of the examined and standard procedures for the investigation of topical solution having Salicylic acid

Pharmaceutical preparation	Rec. * % proposed method	Rec. * % standard method
Sodium Salicylate pure	99.702	100.200
Avomack Topical solution	99.284	98.000
Duofilm Topical solution	100.513	102.000
NOCAL Topical solution	100.513	99.600

* Average for five determinations

4. CONCLUSION

A rapid, precise, sensitive and simple spectrophotometric procedure was been evaluation into the investigation of microgram quantities amounts of sodium salicylate in the hydrous solution depended on the diazotization coupling reaction with para-amino benzoic acid. The law of Beer was Introduced on the range of concentration from 2-30 $\mu g.ml^{-1}$ of sodium salicylate, the sensitivity of sandell index and the molar absorptivity were 0.0188 $\mu g/cm^2$, 8.5013×10^3l mol^{-1} cm^{-1} subsequently, the reaction of sodium salicylate with diazotized para-amino benzoic acid with the ratio for 1:1, the procedure does not need to the control of temperature control and solvent extraction.

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