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Spectrophotometric Determination of Sodium Salicylate in Pharmaceutical Preparations by Coupling with Diazotized Para-Amino Benzoic Acid

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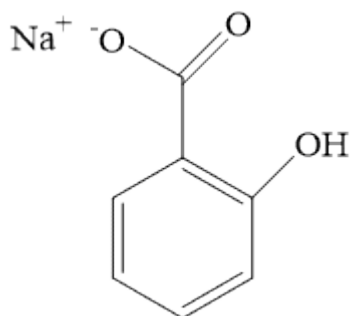
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Abstract- A rapid, sensitive and simple spectrophotometric procedure for the assay of the smaller amounts measures from sodium salicylate at pharmaceutical preparations (topical-solution) was examined. The procedure is focus on a diazotization and 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) $\mu\text{g}.\text{ml}^{-1}$ of sodium salicylate, the molar absorptivity and the sensitivity of Sandell index were $8.5013 \times 10^3 \text{ l mol}^{-1} \text{ cm}^{-1}$, $0.0188 \mu\text{g}/\text{cm}^2$ subsequently, The procedure does not need to the control of temperature and the extraction by the solvent. The perfect circumstances for all colour increasing are portrayed and the examined procedure has been very good application on the assay of sodium salicylate at topical- solution preparations. The general excipients materials and additives did not affect the examined procedure.

Keywords: diazotization coupling reaction, spectrophotometric determination, sodium salicylate, para-amino benzoic acid.

I. INTRODUCTION

Sodium salicylate is the crystalline powder and white or almost white colour, or crystals with small, colourless or flakes shiny, water freely soluble, ethanol sparingly soluble (96per cent).It is a sodium 2-hydroxybenzene carboxylate, $\text{C}_7\text{H}_5\text{NaO}_3$, where as its chemical structure is ^[1]



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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.^[2]

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 ^{[3][4][5]} and otherwise necrosis.^[6] It was using as Potential alternative for aspirin drug that was giving to sensitive people for this drug .It may additionally be utilized as a phosphor for the discovery of vacuum ultraviolet radiation and electrons.^[7]

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 the reaction (azo-coupling) in basic medium. The serious splendid yellow that was resulting in the product .it was spectrophotometrically computed at 452 nm. The new analytical method is accurate, rapid and simple. The procedure was making a very good application in the investigation for sodium salicylate in pharmaceutical preparations(topical-solution).

II. EXPERIMENTAL

a) Apparatus

- every absorbance and spectral estimations were performed on double - beam applied UV-Visible 160 digital recording spectrometer (japan).
- Heating-cooling water bath (Haake, Fe3).
- Analytical balance (Sartorius BL 210S).
- pH meter, Jenway 3020.

III. MATERIAL AND REAGENTS

The Chemical substances that were utilized in the procedure with very high purity degree and did not

required to purification, all solutions were obtained by the next steps .

a) *Sodium salicylate (500 $\mu\text{g}.\text{ml}^{-1}$) solution*

This solution is supplied by dissolution for (0.05g) of sodium salicylate (SDI) in(100 mL deionized water. This solution is at that point exchanged to a dim bottle where it is steady for no less than 1 month ^[1].

b) *Para-amino benzoic acid (3 $\times 10^{-3}\text{M}$) (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 shaken well, then Continued by adding of (0.009 gm) from sodium nitrite (BDH) shake completely, 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.

c) *Hydrochloric acid (BDH) (1M)*

It was provided by dissolution reasonable measure of concentrated hydrochloric to (100 mL) by deionized water.

d) *Sodium hydroxide (BDH) (0.5M)*

It was supplied by dissolution (2.0 gm) of sodium hydroxide at (100 mL) volumetric flask, the volume was completed to the lebal with deionized water.

Procedure:

Separately, volumetric flasks (25mL), the volumes was increasing of (500 $\mu\text{g}.\text{ml}^{-1}$) sodium salicylate from the standard working solution were exchanged to cover a range between (2-30) $\mu\text{g}.\text{ml}^{-1}$ 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 measured at 452 nm against a blank reagent that was including all 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 mark with deionized water. An aliquot for this solution (1mL) was put in volumetric flask (25 mL), (2mL) (0.003M) diazonium agent, 1mL(0.5M NaOH), that were adding, the completed volume to the lebal 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 was giving in the following:

- 1- *Avomack topical –solution (MECP.Riyadh-KSA):* containing 16.7% w/w Salicylic acid according to the product label.
- 2- *Duofilm topical – solution (ITD,Sligo,IRELAND):* containing 16.7% w/w Salicylic acid, according to the product label.
- 3- *NOCAL topical – solution (JORDAN):* containing 10% w/w Salicylic acid, as indicated by the item mark.

Furthermore, the % Salicylic acid produced by the suggested technique is as per the following.

Table (1) : Salicylic acid investigation in some pharmaceuticals by utilizing the suggested technique:

المستحضر الصيدلاني	Conc. Salicylic Acid $\mu\text{g}.\text{ml}^{-1}$		E %	Rec. %	RSD % n=5	Conc. Sod.Salicylate $\mu\text{g}.\text{ml}^{-1}$ *
	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.

IV. RESULTS AND DISCUSSION

The perfect reaction circumstances was studied, The impacts of different parameters on the

optical characteristics for the azo colour have been examined and the reaction circumstances are given.

- 1- *Reagent volume effect*:- The diazonium reagent (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.
- 2- *Acid volume effect*:- the presence of acid that was adding in the suggested procedure resulted in a 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.
- 3- *Base volume effect of*:- 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 ammonium hydroxide sodium hydroxide, sodium acetate, sodium carbonate and potassium hydroxide. highly stability and sensitivity were given just when the reaction was performed with the attendance of sodium hydroxide solution. The various concentrations of NaOH effect were examined, (0.1-4 M) volumes 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.
- 4- *Order Addition effect*:- the ideal order of addition that obtains the maximum absorption was (D+B+R) wherever (B=base, D=drug substance and R=reagent) which was choosing in the following experiments.
- 5- *Temperature effect*:- The produced compound the 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 (0-70) $^{\circ}\text{C}$, 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 - 20) $^{\circ}\text{C}$. so that, this range of temperature was chosen in examined procedure.
- 6- *Reaction Time effect*:- 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 ^[8]and (1M) concentration for hydrochloric acid was chosen ^[9], the absorbance for the colour compound formed has been highly stable and intense in basic medium ^[10],

a) *Absorption spectra*^[11]

The dilute solutions from sodium salicylate in under the the foregoing from the 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. 1) gives the spectra of absorption. The highly absorption wavelength was at 452nm. it was yet utilized for the next determinations.

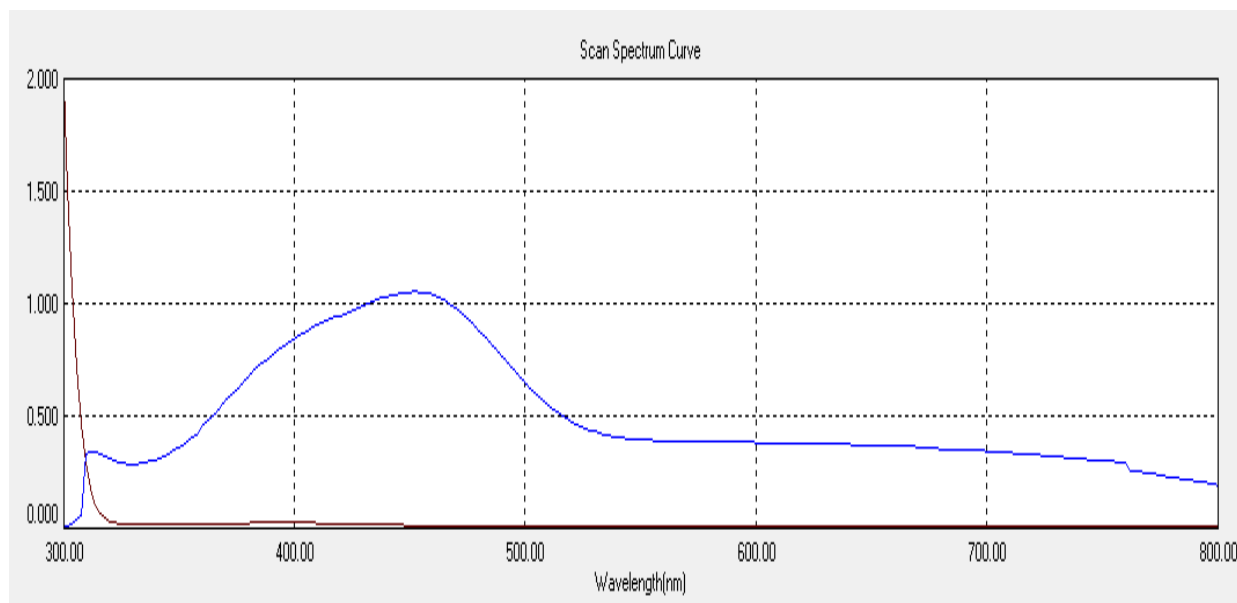


Fig (1) : The spectra of absorption:

A : sodium salicylate ($20 \mu\text{g. ml}^{-1}$) + para-amino benzoic (3×10^{-3}) (product compound) versus the reagent (blank).
 B : the Blank reagent solution versus D.W.

b) Calibration curve^[12]

By using the established practical circumstances, the linear relationship between the concentration of sodium salicylate and the absorbance was noted during the range of concentration (2-

$30 \mu\text{g. ml}^{-1}$) (Fig 2) and a correlation coefficient and the intercept were 0.9990, 0.0821 Respectively. The beer's law was given negative deviation at the concentrations up to ($30 \mu\text{g. ml}^{-1}$) from the sodium salicylate. The molar absorptivity was $8.5013 \times 10^3 \text{ l. mol}^{-1} \cdot \text{cm}^{-1}$.

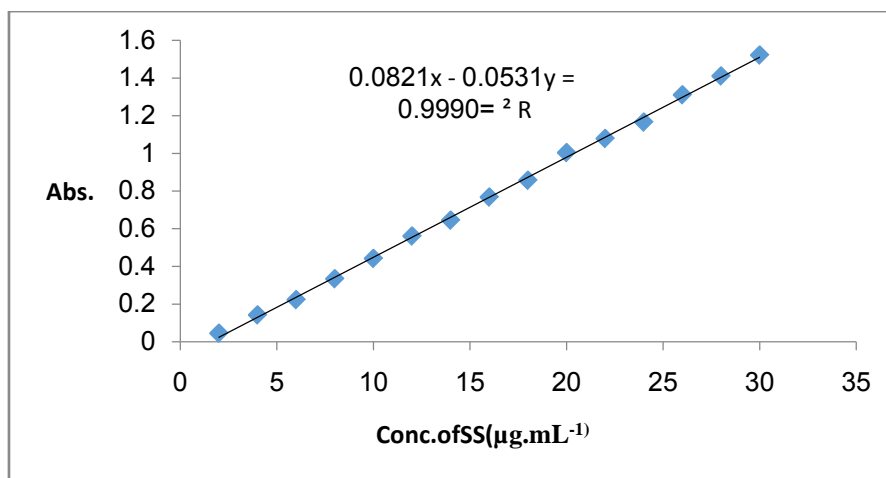


Fig (2) : calibration curve of sodium salicylate(ss)

c) Precision and accuracy^[13]

To investigate the precision and accuracy of the calibration curve, sodium salicylate was designated at three various concentrations. The results appeared in Table (2) was demonstrated a good satisfactory accuracy and precision.

Table (2) : Precision and accuracy of examined procedure

No.	Conc. of sodium salicylate mg per 25ml		Error %*	Recovery*	R.S.D %*
	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

d) Product nature of and the mechanism of reaction^[14,15]

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 a ratio of 1:1, Fig (3&4), demonstrating a mono azo colour with possibly of the next schema:

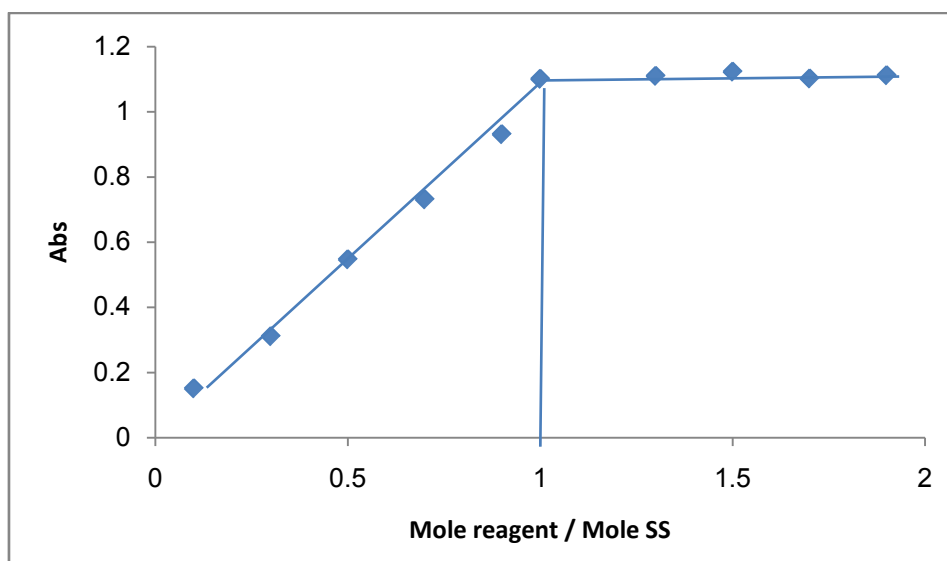
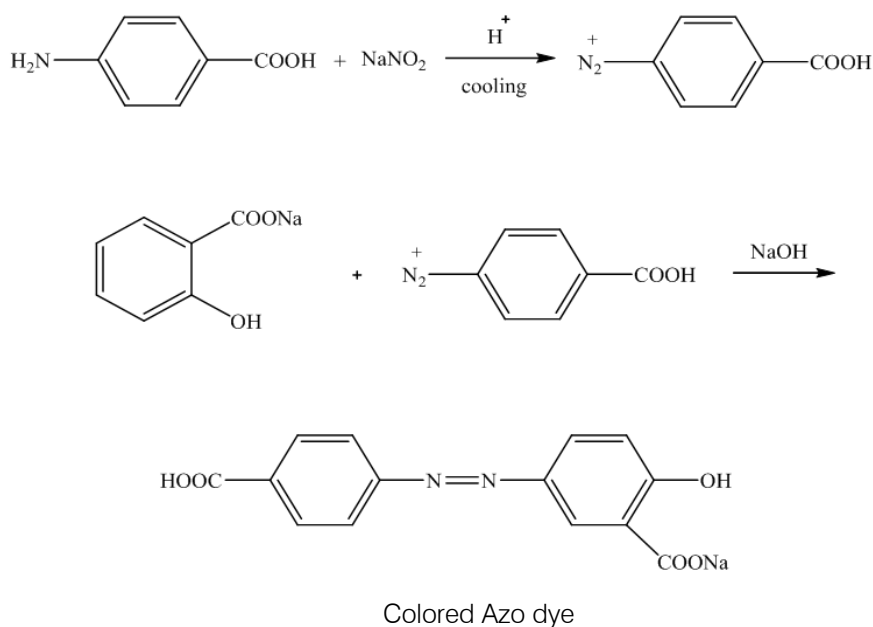
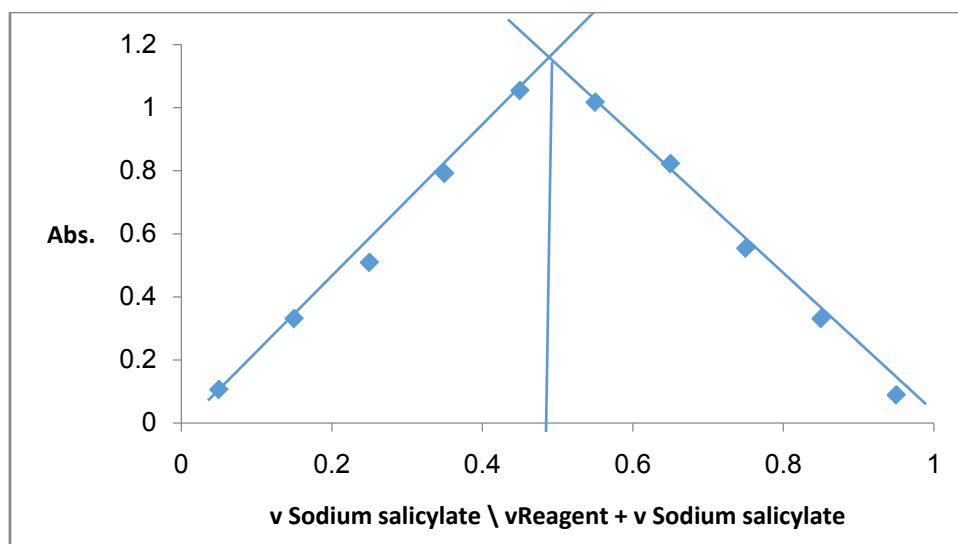


Fig (3) : Mole ratio plot



Fig(4) : Continuous variation plot

The stability constant was computed for the azo dye in the aqueous solution, by using the circumstances of practical method, the constant was equal to $.28 \times 10^6$ l.mole⁻¹.

The regression equation was given, and the analytical data for this method are obtained in the next (Table 2).

Table(3) : Analytical properties of the developed method for the investigation of sodium salicylate

Parameter	studied method
Regression equation	$Y=0.0531x-0.0821$
Linear range($\mu\text{g ml}^{-1}$)	2-30
Correlation coefficient, r^2	0.9990
Detection limit ($\mu\text{g ml}^{-1}$)	0.064
Average of recovery %	99.702
Average of RSD) %	0.854
Sandell's sensitivity ($\mu\text{g cm}^{-2}$)	0.0188
Molar absorptivity ($\text{l mol}^{-1} \text{cm}^{-1}$)	8.5013×10^3

e) Interferences effect^[16]

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 ($20\mu\text{g.ml}^{-1}$) of Salicylic acid by utilizing the studied procedure have been tested, the results are obtained in Table(3).

Table (4) : Excipients effect on the investigation of ($20\mu\text{g.ml}^{-1}$) of Salicylic acid

Exeipient	Conc.of Salicylic acid $\mu\text{g.ml}^{-1}$	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 vinylpyrrolidone(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

f) *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, they

was obtaining a better precision and accuracy as appeared in (Table 5). The examined procedure were given successful comparison with the standard procedure ^[1].

(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

V. CONCLUSION

A sensitive, simple, rapid and precise spectrophotometric procedure has been evaluation for the investigation of microgram quantities of sodium salicylate in the aqueous solution depended on the diazotization reaction coupling with para-amino benzoic acid ,the procedure does not need to the control of temperature control and solvent extraction.

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