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Article · February 2020

DOI: 10.31838/ijpr/2020.12.01.039

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ISSN 0975-2366
DOI:https://doi.org/10.31838/ijpr/2020.12.01.039

Research Article

Spectrophotometric Evaluation of Paracetamol in Bulk and Pharmaceutical Preparations

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Received: 16.10.19, Revised: 17.11.19, Accepted: 22.12.19

ABSTRACT

An uncomplicated, new and sensitive spectrophotometric technique for determining paracetamol was presented in this research article. The suggested technique includes the reacting Sodium nitrite ($NaNO_2$) with hydrochloric acid to yield nitrous acid (HO-NO) and the acid reacting with paracetamol in a hydrochloric acid medium for producing orange colored product with an extreme absorbing at 431.0 nm. There haven't any observed interferences from the typical excipients in the formulations. The technique is efficaciously engaged for the determining paracetamol in numerous medicinal formulations. The fallouts have statistically compared with gotten results based on the official technique.

Key words: Paracetamol, Spectrophotometry, Sodium nitrite, Hydrochloric acid.

INTRODUCTION

Paracetamol (N-acetyl-p-aminophenol) has been extensively used as analgesic and antipyretic drug consumed for the fever relief, minor aches in addition to pains and headaches, with ibuprofen, caffeine and diclofenac sodium. Their determining in drugs is of dominant prominence, as the paracetamol overdose can generate fulminating hepatic necrosis and other poisonous effects[1-2]. These drugs are within category of aniline analgesics Many testified approaches in the literature require costly reagents and consuming time. Spectrophotometric determination is an uncomplicated, speedy and sensitive analytical technique for quantitative analysis that offers realistic and substantial cost-effective benefits as compared with other methods. Consequently, they have numerous options for pharmacological analyses[3]. Numerous analytical approaches were proposed for determining paracetamol. In literature, many techniques have been presented for assay of paracetamol in diverse categories of samples involving pharmacological preparations like chromatographic [4-16], spectrophotometric [17-34], Voltammetry [35-44], Electrochemical [45-49], The goal of the this paper is to present uncomplicated spectrophotometric analytical approaches for determining paracetamol for pharmacological preparations.

EXPERIMENTAL

Apparatus

A Cecil model CE-7200 ultraviolet–visible (UV/Vis) spectrophotometer with 1.0 cm matched cells has been employed to investigate electronic spectral measurements.

CHEMICALS AND REAGENTS

Materials

Every employed chemical has been within analytical reagent grade and paracetamol criterion with (99 % purity) gotten from the state Company for Drugs Industry and Medical Appliances Samarra Iraq (SDI).

1. A stander solution of (500 µg/ml) paracetamol has been freshly organized through dissolving 0.05 g of paracetamol in 10 ml of distilled water. Thenceforward, it has diluted to a mark by the similar solvent in volumetric flask 100 ml.
2. Sodium nitrite (1.0 %) has been organized through dissolving 1.0 g in distilled water and diluted to the mark with the identical solvent in the volumetric flask 100 ml.
3. Hydrochloric Acid solution (1.0 M) has been organized by transfer of 4.25 ml from concentrated acid and diluted up to a mark with purified water in volumetric flask 50.0 ml.
4. Sulfamic acid (0.50 %) has organized through dissolving 0.50 g sulfamic acid in distilled water and complete to a mark in volumetric flask 100 ml with purified water.
5. Sodium Hydroxide (1.0 M) has organized through dissolving 4.0 g NaOH in distilled

water and after that diluted up to a mark in volumetric flask of 100 ml based on the similar solvent.

6. Acetic acid (1.0 M) has been organized as a result of 5.75 ml taking of concentrated CH_3COOH and diluted to 100 ml with purified water.
7. Sulfuric acid (1.0 M has been organized as a result of 5.44 ml taking of concentrated H_2SO_4 and diluted to 100 ml with purified water.
8. Glucose (10000 µg/ml) has been organized as a result of 0.25 g of glucose dissolving in 25 ml distilled water.
9. Sucrose (10000 µg/ml) has been organized as a result of 0.25 g of lactose dissolving in 25 ml distilled water.
10. Lactose (10000 µg/ml) has been organized as a result of 0.25 g of lactose dissolving in 25 ml distilled water.
11. Vanillin (10000 µg/ml) has been organized as a result of 0.25 g of vanillin dissolving in 25 ml methanol.
12. Starch (10000 µg/ml): Triturate a soluble starch 0.25 g using a slight cold water into a thin paste. Then, insert 25 ml of boiled water. Boil up to a clear solution can be gotten for 5 min. This solution must be newly organized as necessary [50].

Solution for the analyzing paracetamol in pharmacological preparations

i. In Tablets

The 10 tablet content has grinded and mixed appropriately. A definite quantity of the fine powder has been precisely weighted for giving 500 mg for tablet, dissolved in 50 ml of distilled water, swirled, leaved to stand for 5 min. Then, it has diluted to 100 ml in the volumetric flask with purified water. The solution has processed via whatman filter paper No.41 for avoiding undissolved and suspended materials before use. The primary filtrate portion has been rejected. By the way, syrup and ampule employed solutions have freshly organized by consequent dilutions with purified water, and investigated based on the recommended procedure.

ii. In Syrup

Every 5 mL of the syrup has 250 mg of paracetamol. The precisely measured 1.0 ml volume has conveyed into the 100 ml volumetric flask. Afterward, insert 50 ml of distilled water swirled, left to stand for 5 min. and diluted up to the mark with distilled water to become 500 µg/ml paracetamol solutions. A solution has filtered via Whatman filter paper No.41 to dispose of undissolved and suspended elements prior to use. The primary filtrate portion has been rejected. By the way, syrup and ampule employed solutions have freshly organized by consequent dilutions with purified water, and investigated based on the recommended procedure.

iii. In Vail and ampoule

Each vail or ampoule contains 100, 300, 600 mg of paracetamol. A precisely measured volume has been transferred into the 100 ml volumetric flask, then supplementary 50.0 ml of distilled water swirled, left to tolerate 5 min. and diluted to the mark with purified water to obtain 500 µg/ml paracetamol solutions. Employed solutions have been newly primed through consequent dilutions with purified water, and examined using the suggested procedure.

RESULTS AND DISCUSSION

Determination of Wavelength Maximum (λmax)

To determine the λmax, an aliquot of the typical solution (500 µg/ml) having 500 µg of paracetamol has been conveyed to 10.0 ml volumetric flask. After that, 1 ml of sodium nitrite (1.0 %) and 0.25 ml of (1.0 M) HCl solution have been inserted. The contents have mixed well and leaved to stand for 5.0 min. After that, 0.1 ml of sulfamic acid (0.5 %) has inserted added carefully to neutralize excess nitrous acid, and leaved to stand for 20.0 min., then 2.0 ml of sodium hydroxide (1.0 M) were added and the absorbing of the colored product has read in contradiction of reagent blank within 400-600 nm range. The extreme absorption wavelength for colored product has been 431.0 nm based on Fig 1. All reagent blank has depicted a trivial absorbance at the corresponding λmax under the tentative conditions.

The proposed mechanism

The orange colored product obtained after react paracetamol with an electrophilic of nitrous acid in the presence of acidic medium. The following mechanism has explained of the reaction as shown in scheme (1).

Optimizing reaction variables

With the intention of establishing optimal investigational conditions for swift and measureable formation of colored product with supreme stability and sensitivity, the consequence of numerous factors like volumes of sodium nitrite (1.0 % w/v), volumes of hydrochloric solution (1.0 ml), first reaction time, volumes of sulfamic acid (0.5 % w/v), second reaction time and volumes of sodium hydroxide (1.0 M). A stability of colored product has been investigated at 25 ℃ for room temperature.

Optimization of the Experimental Conditions

The finest experimentation conditions have been started by changing single parameter and perceiving its influence on the absorbance of colored species.

Influence of Volume of Sodium nitrite

The effect of sodium nitrite volume on the forming of colored product has examined. Varying volumes of standard (1.0 % w/v) sodium nitrite solutions in the range (0.25 - 3.0 ml) were added and measuring the absorbance's of the solutions. The test has depicted that 1.0 ml of sodium nitrite solution gave maximum absorbance (Fig 2).

Influence of different acids on the reaction

The influence of dissimilar acid for the reaction product like hydrochloric acid, sulfuric acid, nitric acid and acetic acid on the formed colored product has investigated. 1.0 ml from an acids of standard (1.0 M) were added and measuring the absorbance's of the solutions. The investigation showed that hydrochloric acid solution gave maximum absorbance as shown in table 1.

Influence of Volume of hydrochloric acid on the reaction

The consequence of hydrochloric acid volume for the formed colored product has examined. Varying volumes of standard (1.0 M) HCl solutions in the range (0.1 – 2.0 ml) were added and measuring the absorbance's of the solutions. The investigation showed that 0.25 ml of HCl solution gave the highest absorbance as depicted by Fig 3.

Influence of First Time on The Reaction

The consequence of time on the color intensity of the reaction at different time (0-30 min) was studied by measuring the absorbance at room temperature (25±1°C). It was found that the reaction got maximum absorbance at 3.0 min. and the value start to decrease gradually when reaction time raised above 3.0 min as stated by table 2.

Influence of Volume of Sulfamic acid

The consequence of sulfamic acid volume on the formation colored product was studied. Varying volumes of standard (0.5 % w/v) sulfamic acid solutions in the range (0.005 – 1.5 ml) were added and measuring the absorbance's of the solutions. The investigation showed that 0.1 ml of sulfamic acid solution gave hugest absorbance based on Fig 4.

Influence of Second Time on the Reaction

The consequence of second time on the color intensity of the reaction at different time (0-30 min) was studied by measuring the absorbance at room temperature (25±1°C). It was found that the reaction got maximum absorbance at 20.0 min. and the value start to decrease gradually when reaction time raised above 20.0 min as stated by table 3.

Consequence of diverse bases on the reaction

The influence of dissimilar bases on the reaction product such as (sodium hydroxide, ammonium hydroxide, potassium hydroxide and sodium bicarbonate) on the formed colored product has examined. About 2.0 ml from a base of standard (1.0 M) were added and measuring the absorbance's of the solutions. The investigation has depicted that sodium hydroxide solution gave highest absorbance as shown in table 4.

Consequence of Volume of sodium hydroxide on the reaction

The consequence of sodium hydroxide volume on the formation colored product has been tested. Varying volumes of standard (1.0 M) NaOH solutions in the range (0.25 – 3.5 ml) were added and measuring the absorbance's of the solutions. The 2.0 ml of sodium hydroxide solution has given the greatest absorbance as detected by Fig 5.

Consequence of Order Addition of Reactants

Intended for obtaining the optimal results, the addition order of reagents must be as in the procedure below. Otherwise, a color intensity loss can be perceived.

General Procedure and Calibration Graph

By adopting 10 ml volumetric flasks, 0.05 to 1.0 mL of 500 µg/ml of paracetamol have been inserted, 1.0 ml of sodium nitrite (1.0 %) has inserted and followed by 0.25 ml of HCl (1.0 M). The resulted mixtures were shaken well and leaved to stand for 5.0 min. Then add 0.1 ml of sulfamic acid (0.5 %), and leaved to stand for 20.0 min, then 2.0 ml of sodium hydroxide (1.0 M) were inserted, the volume has accomplished up to the mark with purified water, and the resultant solution has determined at 431.0 nm in contradiction of reagent blank treated in the same way. The calibration curves for paracetamol showed excellent linearity at concentration ranges of (2.5 -50.0 µg/ml) based on Figure 6.

Spectral Features of the Suggested Method

Molar absorptivity, Beer's Law and Sandell's sensitivities for paracetamol are given in Table 5 based on described experimental conditions.

Precision and Accuracy of the Suggested Technique

The precision of the planned approach has done based on replicate analysis of 5 distinct sample solutions at three paracetamol concentration levels. The relative standard deviations (RSD %) have been 0.0632-0.168 %, on the other hand the accuracy of the suggested approaches has evaluated by calculating the relative error percentage (R.E %) table 6. The consequences

indicated worthy method accuracy at each concentration level.

Interference Investigation

The fallouts of interferences investigation have shown that no interferences have been existing from the excipients of studied glucose, sucrose, lactose, starch and vanillin. The recovery of paracetamol was ranged 99.42- 101.50 %. Table (7) specified the nonappearance of interferences for these excipients.

Application of the Suggested Technique for Analyzing Paracetamol in pharmaceutical Formulation

To increase the insurance, the suggested spectrophotometric process has employed for determining paracetamol in pharmaceutical preparation sample. Table (8) shows the result of accuracy based on relative error percent, and reveals that the process has been reasonably accurate.

CONCLUSION

The projected approach for determining paracetamol experimentally and pharmacologically has been uncomplicated, inexpensive, sensitive and speedy. The Statistical considerations and the recovery investigation data noticeably specify the accuracy and reproducibility of the technique. The suggested process is appropriate for the assay and drugs evaluation in pharmacological productions to guarantee huge standard of quality control.

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Table 1: The consequence of dissimilar acids on the reaction product.

	Acid	Absorbance
	HCl	0.573
	H_2SO_4	0.563
	HNO_3	0.555
	CH_3COOH	0.511

Table 2: The consequence of first time in the reaction product.

Time (min)	Absorbance
0	0.522
3	0.560
5	0.586
10	0.577
12	0.576
15	0.566
20	0.565
25	0.563
30	0.561

Table 3: The consequence of second time on the reaction product.

Time (min)	Absorbance
0	0.532
3	0.553
5	0.586
10	0.587
15	0.589

20	0.595
25	0.580
30	0.571

Table 4: The consequence of dissimilar bases on the reaction product

Type of Basic Medium	Absorbance
NaOH	0.595
KOH	0.553
NH_4OH	0.527
$NaHCO_3$	0.455

Table 5: The Optical features and statistical information for determining paracetamol.

Parameter	Value
λ_{max} (nm)	431
Color	Yellow
Linearity range (µg/ml)	2.5 – 50
Molar absorptivity(L/mol.cm)	4367.2524
Regression equation	Y= 0.0289X + 0.0113
Calibration Sensitivity(L/ mg)	0.0289
Sandal's Sensitivity ($\mu g/cm^2$)	0.0346
Correlation of Linearity (R^2)	0.9999
Correlation coefficient (r)	0.9999
Detection limit LOD (µg/ml)	0.0204
Quantification limit LOQ (µg/ml)	0.0309

Table 6: Precision and Accuracy for the suggested approach

Paracetamol Conc. (µg/ml)		Relative Error%	S.D	R.S.D.* %
Taken	Found*			
15	14.9723	- 0.1846	0.0252	0.168
20	20.1811	0.9055	0.0245	0.121
40	40.0242	0.0605	0.0253	0.0632

* Average of three determinations.

Table 7: The effect of the existence of (1000 µg/ml) from the excipients on determining the paracetamol 20.0 µg/ml based on the suggested method.

Excipients	Paracetamol Conc. Taken 20 µg/ml	
	Conc. Found* µg/ml	% Recovery
glucose	20.1280	100.640
Sucrose	19.8858	99.4290
Lactose	20.0242	100.121
Starch	20.3010	101.505
Vanillin	19.9896	99.9480

* Average of three determinations.

Table 8: The results of the determination of paracetamol in pharmaceuticals formulation by the suggested technique.

Sample	Labeled amount mg	Found amount mg	Conc. taken µg/ml	Conc.* found µg/ml	Recovery%	S.D*	R.S.D* %
(Paracetamol) 500 mg/ tablet SDI / Iraq	500	497.51	15	14.9146	99.431	0.0582	0.3903
		502.71	30	30.1626	100.54	0.0346	0.1147
Parokan: vial 0 mg/ ml /100 ml vial Paracetamo Bekoze / Istanbul	10	10.1353	15	15.2029	101.35	0.0263	0.1729
		10.0514	35	35.1799	100.51	0.1386	0.3939
Ampoule: Hayamalplus. 300 mg / Paracetamol / 20 mg lidocaine HCIlbnhyyan.Syria	300	306.41	20	20.4279	102.13	0.8352	4.0885
		301.911	40	40.2549	100.63	0.0165	0.0411
Ampoule: Injection 600mg/Paracetamol/Mumboiu, India	600	601.764	20	20.0588	100.29	0.1039	0.5179
		605.558	30	30.2779	100.29	0.0902	0.2987
Syrup piodal 5 ml/250mg Paracetamol / Piodal, Iraq	250	245.127	10	9.8051	98.051	0.0799	0.8149
		253.52	25	25.3529	101.41	0.3015	1.1892

*Average of three determinations.

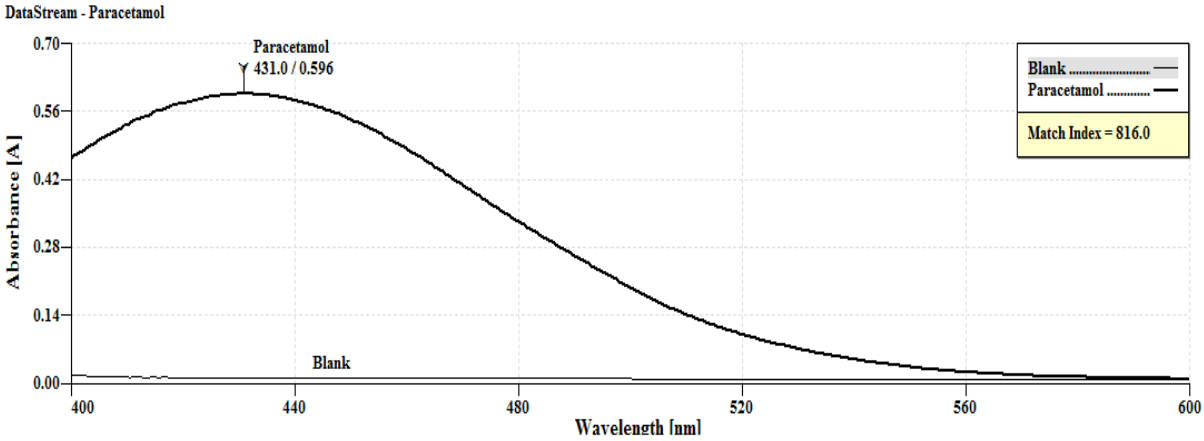


Figure 1: Absorption spectrums of colored reacted product (Paracetamol 20.0 µg/ml) in contradiction of reagent blank.

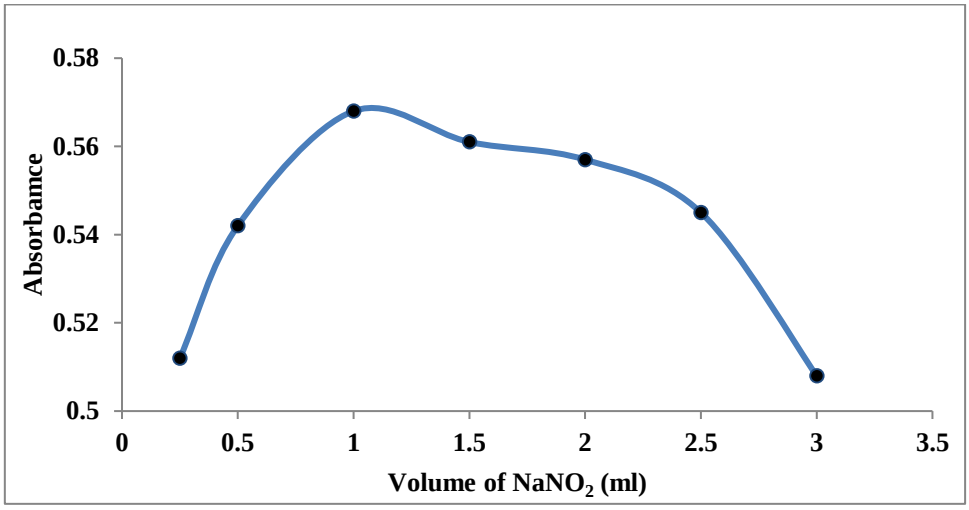


Figure 2: Influence of Volume of sodium nitrite (1.0 % w/v) on the absorbance of the reaction product.

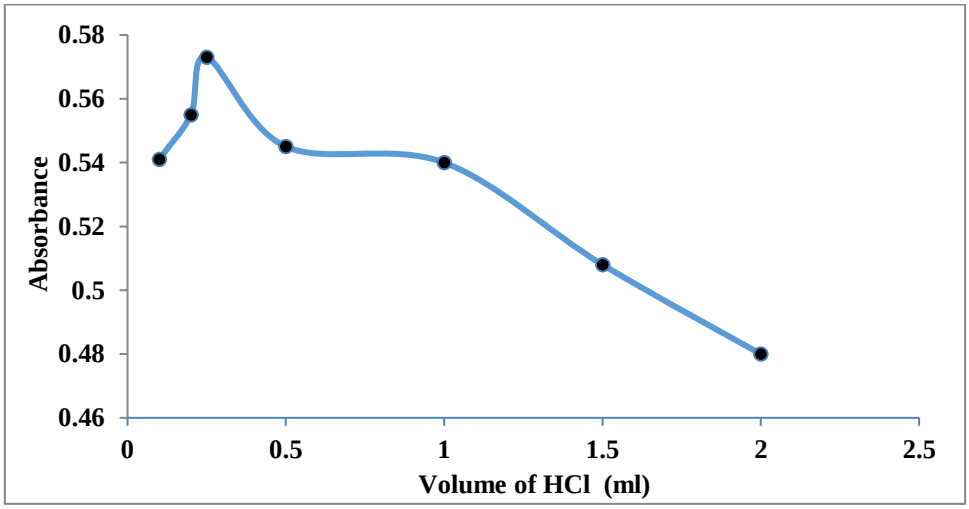


Figure 3: Influence of Volume of hydrochloric acid (1.0 M) on the absorbance of the reaction product.

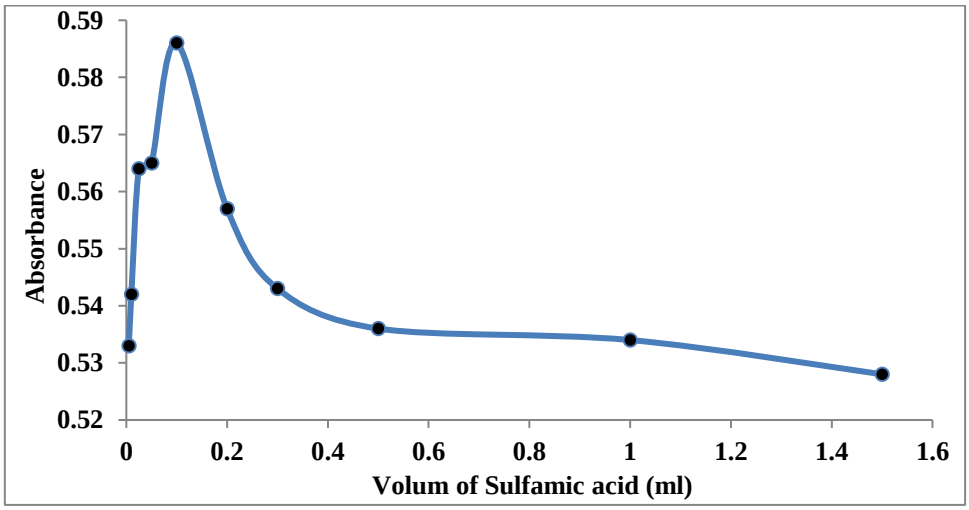


Figure 4: Consequence of volume of sulfamic acid (0.5 % w/v) in the absorbance of reaction product.

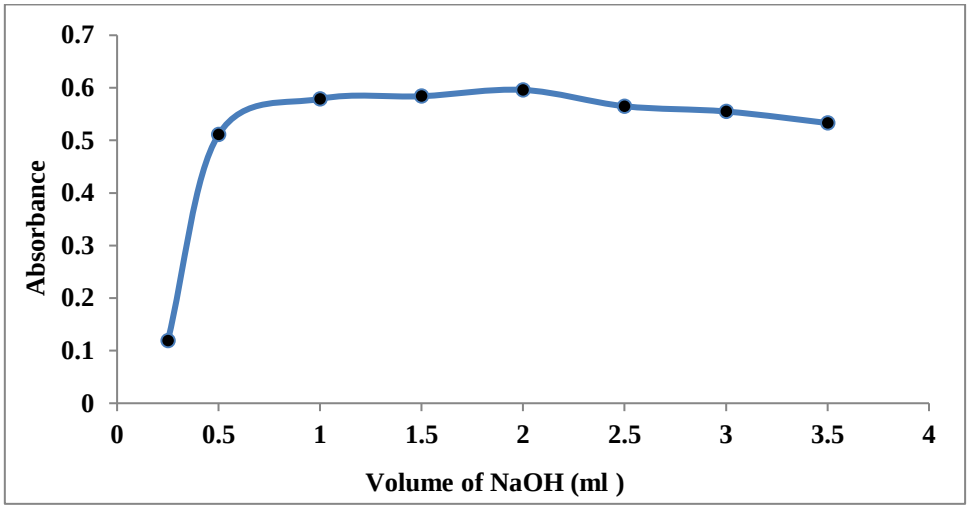


Figure 5: Consequence of Volume of sodium hydroxide (1.0 M) in the absorbance of reaction product.

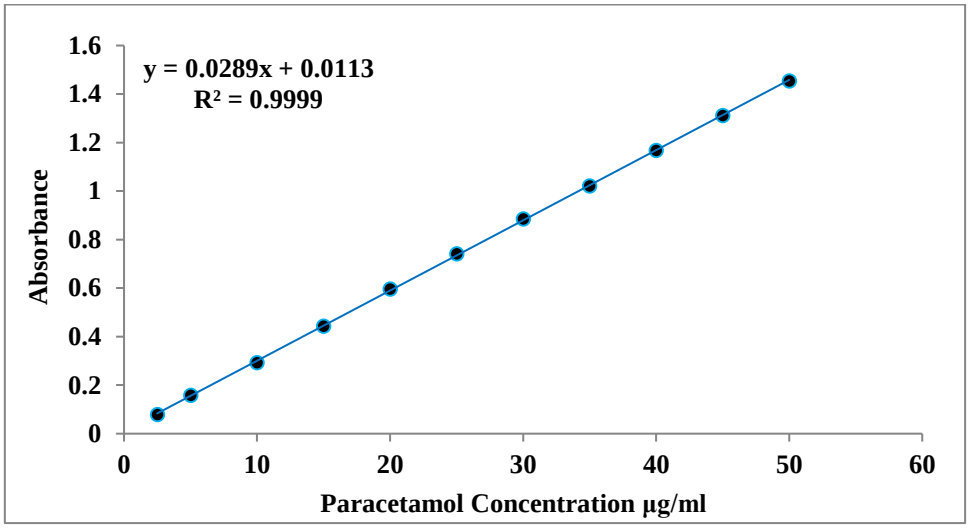
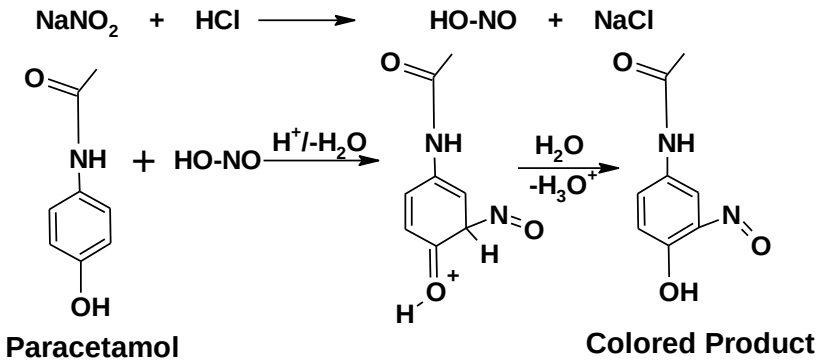


Figure 6: Calibration result of paracetamol of resulting product.



Scheme (1): The reaction mechanism of the proposed method.