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Spectrophotometric Determination of Bisacodyl in Pure and Pharmaceutical Preparation via Oxidative Coupling Organic Reaction

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Abstract:

A simple, accurate and sensitive spectrophotometric way is used to determine Bisacodyl in pure and pharmaceutical preparations. The proposed method depends on using 2,4-Dinitrophenylhydrazine as chromogenic reagent . The method was based on the oxidative coupling reaction of Bisacodyl with 2,4-Dinitrophenylhydrazine with Sodium periodate in the presence of sodium hydroxide as alkaline media to form red water soluble dye product , that has a maximum absorption at λ_{max} 522nm . Beer 's law is obeyed in the concentration of (2.00–20.00) µg.ml ˉ1 .The molar absorptivity is (6505) $L.mol^{-1}.cm^{-1}$,a sandall sensitivity of(0.0555) $\mu g.cm^{-2}$), correlation coefficient of (0.9970) , Limitof detection (LOD) (0.0312 $\mu g.ml^{-1}$), limit of Quantitation (LOQ) (0. 3125 $\mu g.ml^{-1}$) and the relative standard deviation of RSD% (1.6). The method gave a successful determination for Bisacodyl in pharmaceutical preparations and the value of recovery % was better than (100.16%) .

Key words: Bisacodyl drug, Spectrophotometric determination, Pharmaceutical preparation

Introduction:

Bisacodyl is 4,4` (pyrid - 2 – ylmethylene) bis (phenyl acetate)[$C_{22}H_{19}NO_4$ =361.4] Figure(1) is a laxative used for the treatment of constipation, for evacuation of the colon before radiological of the abdomen, or endoscopy, and before or after surgical operations. It has a little or no action on the small intestine. It stimulates the rectal mucosa, which raises peristaltic movements and causing defecation in 15-30 minutes[1-5] .Doses of 5 to 10 milligrams may be given by mouth and act within 6 to 12 hours.Suppositories of 10 milligrams given by rectum act within one hour.Children under 10 years may be given5 milligrams by mouth or by rectum[6-8]. The literature survey reveals that only few methods have been reported for determination of Bisacodyl in pure form and in pharmaceutiacal

Formulations [9-13]. Bisacodyl has been determined by various pharmacopeial and nonpharmacopeial methods. The official methods involve non aqueous titration for Bisacodyl suppositories, spectrophotometry [14-16].For enteric coated tablets, and high-performance liquid chromatography (HPLC) [17] for both suppositories and enteric
coated tablets. The non pharmacopeial methods for Bisacodyl determination involve spectrophotometry for combinations with piribedil [18].Gas chromatography (GC) in pharmaceutical tablets; GC in urine, serum, and stool [19].

The proposed method is based on the reaction of the Bisacodyl drug with 2,4-dinitrophnylhydrazine in the presence of sodium periodate in alkaline medium to form a red water soluble dye product which gave an absorption maximum at 522 nm.

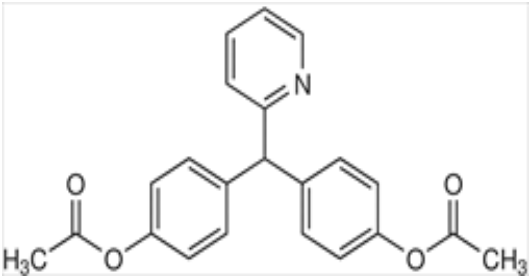


Fig.(1):Chemical Structure of Bisacodyl[20]

Materials and Methods:-

Apparatus

- UV-visible, shimadzu 1700 spectrophotometer, with1.0 cm quartz cells was used for absorption measurements,

-WTW 720 pH meter .

- Electronic balance, sartorius AG gottingen B2 2105 Germany..

Reagents

All chemicals used were of analytical reagent or pharmaceutical grade and distilled water was used throughout the work.

-Stock solutions from drug (1000 µg. ml^{-1}) of Bisacodyl (SDI - Iraq) were prepared by dissolving (1gm) of Bisacodyl in (0.5ml) of concentration sulphuric acid and diluting to the mark in 1000 ml volumetric flask. Working solutions were prepared by diluting the solution in distilled water.

-Stock solution of 2,4-Dinitrophenylhydrazine (0.01M) was prepared by dissolving (0.01980 gm) of 2,4- Dinitro phenyl hydrazine in ethanol and the solution made up to the mark in 100 ml volumetric flask with ethanol.

- Stock solution of Sodiume periodate (0.01M) was prepared by dissolving (0.213 gm) of $NaIO_4$ in distilled water and diluting to mark in 100 ml volumetric flask.

- Stock solution of Sodium hydroxide (NaOH) (1.00 M) was prepared by dissolving(4 gm) of NaOH in distilled water and diluting to the mark in 100 ml volumetric flask and then standardization of this solution with standard solution of HCl .

Procedure for assay of Bisacodyl in pharmaceutical preparations Tablets:

Bisacodyl tablets, provided from (SDI) Samara-Iraq (10) tablets were powdered and a amount of the final powder was accurately weighted to give an equivalent to about 10 mg of Bisacodyl was dissolved in distilled water . The prepared solution transferred to 100 ml volumetric flask and made up to the mark with distilled water forming a solution of 100µg.ml^{-1}concentration. The solution was filtered by Whitman paper to avoid suspended particles. These solutions were diluted quantitatively to form a concentrations in the range of calibration curve.

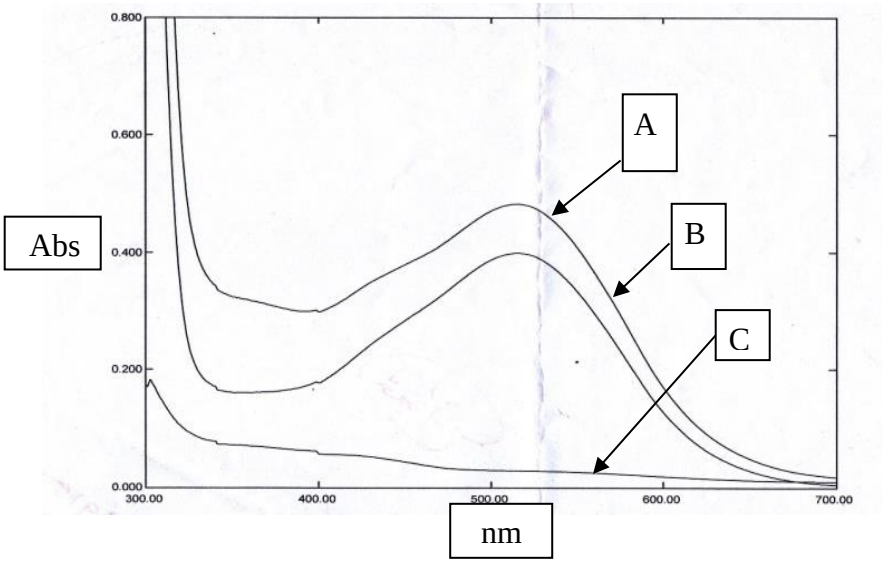
Recommended procedures:

Into a series of 25 ml volumetric flask, transfer an increasing volume of Bisacodyl solution (100 µg.ml^{-1}) to cover the range of calibration curve (2.00 – 20.00) µg.ml^{-1},

added 0.5 ml (0.01 M) of 2,4-Dinitrophenylhydrazine and shake well . Added1.0 ml(0.01M) Sodiume periodate. added 1.0 ml (1.0 M) of NaOH, diluted to the mark with distilled water , and allow the flasks to stand for 30 min at room temperature (25 ºc) . Measure the absorption at(522 nm) against the blank prepared in the same method but no Bisacodyl.

Results and Discussion:

Bisacodyl drug react with 2,4-Dinitro phenyl hydrazine and Sodium periodate in the presence of sodium hydroxide as alkaline media to form an intense red color product that can be measured spectrophotometrically at 522 nmFigure(1).



A:Bisacodyl Vs distilled water
B: Bisacodyl Vs Blank C: Blank Vs distiled water

Fig. (1): Absorption spectra of (A) Bisacodyl versus distilled water (B) Bisacodyl versus Blank (C)Blank versus water.

Study of the optimization Experimental Condition:

The effect of various parameters such as a mount of reactants, order of addition, time and temperature were studied.

Effect of 2,4- Dinitro phenyl hydrazine Volume:

The effect of various volume of 2,4-dinitrophenylhydrazine were investigated. A Volume of (1.4ml) of (0.01M) of reagent show the highest absorbance at 522 nm and was chosed for further use. the results are shown in Figure(2) .

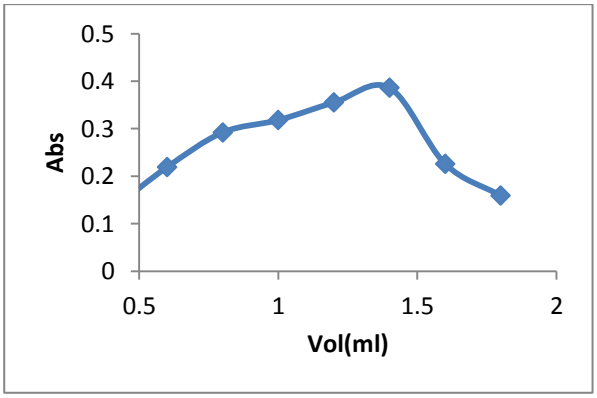


Fig. (2): The Effect of 2,4-Dinitrophenylhydrazine of (0.01M) volume

The Effect of Sodium periodate $NaIO_4$ Volume:

The effect of $NaIO_4$ volume was studied. Avolume of (2 ml) of (0.01M) gave the higher absorption intensity at λ_{max} 522 nm. Figure(3) and thus was selected as optimum volume for further use.

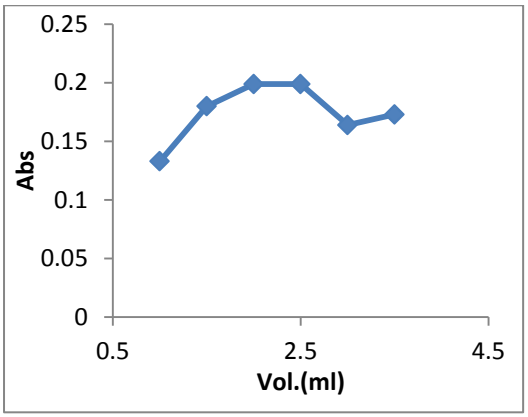


Fig.(3): The Effect of Sodium periodate $NaIO_4$ of (0.01M) volume.

Effect of alkaline media type:

Bisacodyl drug react with Dinitro pheny lhydrazin in the presence of alkaline medias therfore the type of alkaline media is an obtained showed that sodium hydroxide gave the best absorbance Table(1) and was used in the general procedure.

Table (1): The effect of Base media type

Base (0.01)M	Abs.
NaOH	0.386
KOH	0.302
$Ca(OH)_2$	0.285
$Ba(OH)_2$	0.313
NH_4OH	0.318
Na_2CO_3	0.183
$NaHCO_3$	0.201

The Effect of Sodium hydroxide NaOH volume:

The effect of NaOH volume was similarly studied.Avolum of (0.6ml) of (1M) NaOH gave the higher absorption intensity at 522 nm Figure (4).

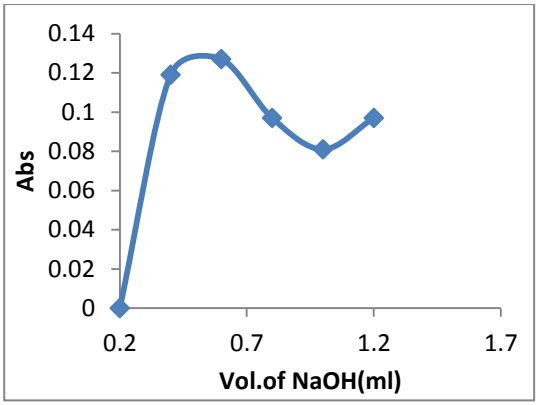


Fig.(4): The Effect of NaOH (1M)Volume

The Effect of order of addition:

The effect of order of reagents addition on the absorption of red product dye was investigated. Table(2) shows the order of addition could be followed,(Drug:2,4-Dintrophenylhydrazin:$NaIO_4$: NaOH). Due to show the highest absorption and thus was selected for further use.

Table (2): The Effect of order of addition.

Order of addition	Absorbance at λ max (522)nm	NO
Drug:2,4 Dintrophenylhydrazin:$NaIO_4$:NaOH	0.398	1
2,4-Dintrophenylhydrazin: Drug:$NaIO_4$:NaOH	0.397	2
Drug: $NaIO_4$:2,4-Dintrophenylhydrazin:NaOH	0.372	3
2,4-Dintrophenylhydrazin: $NaIO_4$:Drug:NaOH	0.231	4
2,4-Dintrophenylhydrazin: NaOH: Drug:$NaIO_4$	0.128	5
Drug: NaOH:2,4-Dintrophenylhydrazin:$NaIO_4$	0.209	6

The Effect of Temperature:

The influence of Temperature on determined color intensity of the product was evaluated in practice the highest absorption was obtained when the product color was developed at (25ºc) Figure(6).

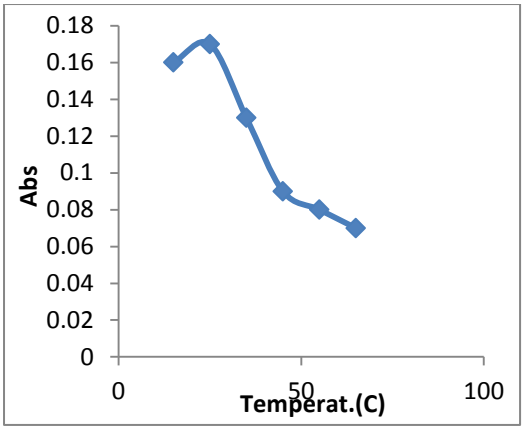


Fig.(6) : The Effect of Temperature

The Effect of reaction Time:

The color intensity reached its maximum absorption after Bisacodyl has been reacted with 2,4-Dintrophenylhydrazin,$NaIO_4$ and NaOH at 10 min . Thus 10 min development time was chosen for further use. The results obtained are shown in Figure (7)

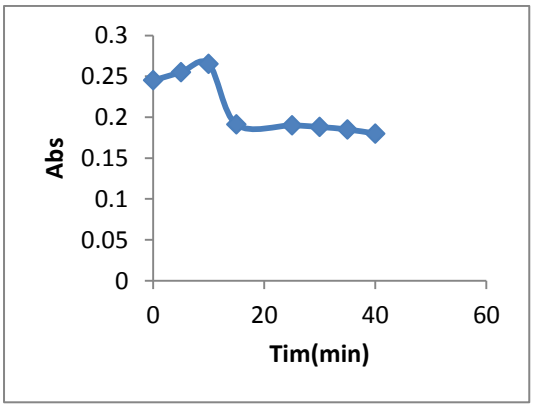


Fig.(7) : The Effect of Time

Calibration Curve:

Using optimum conditions, a linear calibration curve for the determination of Bisacodyl was determined over the concentration range of (2.0 – 20.0) $\mu g.ml^{-1}$. The linear regression equation for the determination of Bisacodyl is (Y= 0.018 X + 0.176) and correlation coefficient of 0.9970 The linear calibration graph is shown in Figure(8).

The statistical treatments of the analytical data are shown in Table(3).

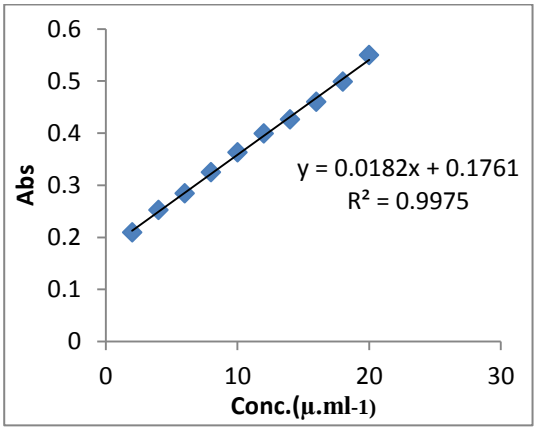


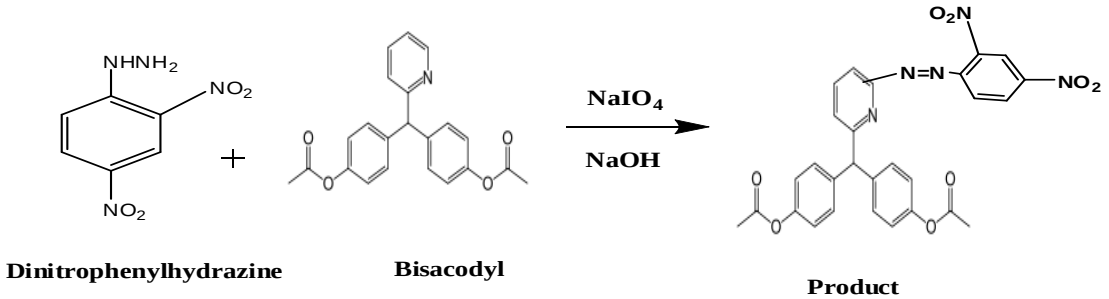
Fig. (8): Calibration Curve for the determination of Bisacodyl .

Table (3): Optical characteristics and statistical data for the determination of Bisacodyl.

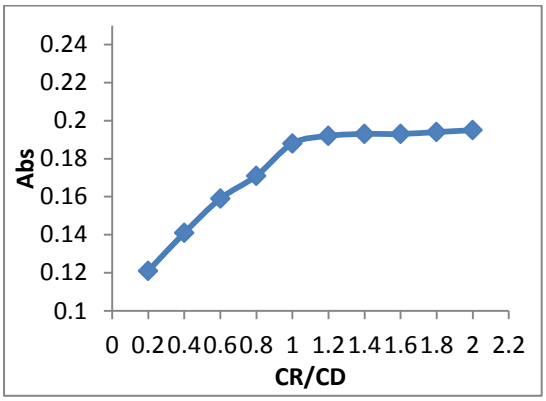
Parameter	value
λ max(nm)	522
Color	red
Linearity range ($\mu g.ml^{-1}$)	2.0-20.0
Regression equation	Y=0.018 X +0. 176
Calibration Sensitivity(ml. μg^{-1})	0.018
Correlation Coefficient (r)	0.9984
Correlation of linearity(R^2)	0.9970
Molar absorptivity ($L.Mol^{-1}.Cm^{-1}$)	6505
Sandells Sensitivity($\mu g.Cm^{-2}$)	0.0555
L.O.D ($\mu g.ml^{-1}$)	0.0312
L.O.Q ($\mu g.ml^{-1}$)	0.3125

Nature of the dye product:

The stoichiometry of the reaction between Bisacody l,2,4-Dinitrohydrazine, $NaIO_4$ and NaOH was investigated using the mole ratio and Slope ratio method [21-24] unsing the optimized conditions. The results in Figure (9), (10), show a 1:1 drug to reagent product were formed. Therefore the formation of the product may probably occurs as follows:

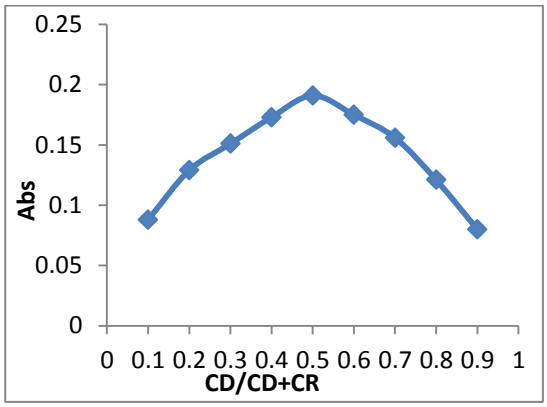


Dinitrophenylhydrazine **Bisacodyl** **Product**



CR:concentration of reagent
CD:concentration of drug

Fig. (9): Molar ratio of drug to reagent



CR:concentration of reagent
CD:concentration of drug

Fig.(10): Continuous *Variation* Method

Analytical Application:

Proposed method has been applied for the determination of Bisacodyl drug in pharmaceutical preparations with good accuracy and precision for the drugs studied. The results obtained were given in Table(4) which confirm Finally, the proposed procedure was compared successfully with the standard procedure Table(3).

Table (4): Application of the proposed procedure for the determination of Bisacodyl in pharmaceutical preparations.

Conc. Of Bisacodyl [µg/ml]	*RE %*	*Recovery %*	*Average recovery %*	*RSD %*
4	***0.24***	*100.24*	*100.16*	*1.6*
8	*0.122*	*100.122*		*0.22*
12	*0.14*	*100.14*		*0.2*

Conclusion:

A simple, accurate and excellent spectrophotometric method was investigated for the determination of Bisacodyl in pure and in pharmaceutical preparations. The proposed method can be carried out with no need for further steps such as solvent extraction step , pH or Temperature control .

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التقدير الطيفي لعقار البسكودايل في المادة النقيةو المستحضرات الصيدلانية بواسطة تفاعلات الاقتران التاكسدي

اقبال سلمان محمد * خنساء احمد ناصر* امل حسين محميد**

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الخلاصة:

يتضمن البحث تطوير طريقة طيفية بسيطة ومضبوطة وحساسة لتقدير العقار بسكودايل في صيغته النقية وفي مستحضراته الصيدلانية.الطريقة المقترحة تعتمد على تفاعل ازدواج البسكودايل مع الكاشف اللوني داي نايتروفنيل هيدرازين وبوجود بيرايودات الصوديوم وهيدروكسيد الصوديوم كوسط قاعدي حيث يتكون مركب لونه احمر يعطي اعظم امتصاص عند الطول الموجي 522 نانوميتر.النتائج اظهرت ان مدى الخطية بين 20.00-2.00 مايكروغرام/مل ومعامل امتصاص مولاري مقداره(6505)) لتر.مول $^{-1}$ سم $^{-1}$ودلالة ساندل مقدارها(0.0555) مايكروغرام.سم $^{-1}$ ومعامل ارتباط (0.9970) وحد كشف نوعي للطريقة (0.0312) مايكروغرام/مل ،وحد كشف كمي (0.3125) ومعدل انحراف قياسي نسبي (1.6).الطريقة طبقت بنجاح لتقدير البسكودايل في المستحضرات الدوائية وبنسبة استرجاعية افضل من (100.16%).

الكلمات المفتاحية: التقدير الطيفي، عقار البسكودايل، المستحضرات الصيدلانية