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

Iqbal S. Mohammed* Khansaa A. Nasser*
Amal H. Mhemeed**

*Department of Chemistry, Diyala University, Diyala, Iraq.
**College of Pharmacy, Misan University, Misan, Iraq.

E-mail: ikbalsalman76@yahoo.com

Received 2/3/2016
Accepted 3/8/2016

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 $\lambda_{\text{max}}$ 522nm. Beer’s law is obeyed in the concentration of (2.00–20.00) μg.ml$^{-1}$. The molar absorptivity is (6505) L.mol$^{-1}$.cm$^{-1}$, a sandall sensitivity of (0.0555) μg.cm$^{-2}$, correlation coefficient of (0.9970), Limit of detection (LOD) (0.0312 μg.ml$^{-1}$), limit of Quantitation (LOQ) (0.3125 μg.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)$[C_{23}H_{19}NO_4 =361.4]$ 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 pharmaceuticcal
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-dinitrophenylhydrazine 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.

![Chemical Structure of Bisacodyl](image)

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

**Materials and Methods:**

**Apparatus**
- UV-visible, shimadzu 1700 spectrophotometer, with 1.0 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 Sodium periodate (0.01M) was prepared by dissolving (0.213 gm) of NaIO₄ 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. Added 1.0 ml (0.01M) Sodium 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 nm Figure(1).

\[ \text{Abs} \]
\[ \text{nm} \]

A: Bisacodyl Vs distilled water
B: Bisacodyl Vs Blank  C: Blank Vs distilled 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).

\[ \text{Abs} \]
\[ \text{Vol(ml)} \]

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. A volume of (2 ml) of (0.01M) gave the higher absorption intensity at $\lambda_{\text{max}}$ 522 nm. Figure(3) and thus was selected as optimum volume for further use.

Effect of alkaline media type:
Bisacodyl drug react with Dinitrophenylhydrazin in the presence of alkaline media 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$_4$OH    | 0.318|
| Na$_2$CO$_3$| 0.183|
| NaHCO$_3$   | 0.201|

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

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 $\lambda_{\text{max}}$ (522nm) | 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).
The Effect of Reaction Time:
The color intensity reached its maximum absorption after Bisacodyl has been reacted with 2,4-Dinitrophenylhydrazine, NaIO₄ and NaOH at 10 min. Thus 10 min development time was chosen for further use. The results obtained are shown in Figure (7).

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) μg.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).

Figure (6): The Effect of Temperature

Figure (7): The Effect of Time

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

| Parameter                      | value  |
|--------------------------------|--------|
| λ max (nm)                     | 522    |
| Color                          | red    |
| Linearity range (μg.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(R²)   | 0.9970 |
| Molar absorptivity (L.Mol⁻¹.Cm⁻¹) | 6505  |
| Sandells Sensitivity(μg.Cm⁻²)  | 0.0555 |
| L.O.D (μg.ml⁻¹)                | 0.0312 |
| L.O.Q (μg.ml⁻¹)                | 0.3125 |

Nature of the dye product:
The stoichiometry of the reaction between Bisacodyl, 1,2,4-Dinitrohydrazine, NaIO₄, and NaOH was investigated using the mole ratio and Slope ratio method [21-24] using 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:
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 % |
|---------------------------|------|------------|--------------------|-------|
| 1.6                       | 0.24 | 100.24     | 100.16             | 1.6   |
| 0.2                       | 0.122| 100.122    |                    | 0.22  |
| 0.122                     | 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.

References:
[1] Metwally, F.; Abdelkawy, M. and Naguib, I. 2007. Development and validation of three stability-indicating methods for determination of bisacodyl in pure form and pharmaceutical preparations. JAOAC Int., 90(10):113–27.
[2] Parfitt, K.; Blake, SC.; Parsons, PS. and Martindale, AV. 2005. The Extra pharmacopeia, 32nd edition, pharmaceutical press: London, 1251P.
[3] Rachmilewitz, D.; Karmeli, F. and Okon, E. 1980. Effect of bisacodyl on CAMP and Prostaglandin E2.
content, (Na+k). ATP ase, adenylylclase, and phosphodiesterase activities of rat intestine. Dig Dis sci., 25(8):602-607.

[4] Bradshaw, K.; Burnett, J. and Sidhu, A. 1995. Highperformance liquid chromatographic determination of bisacodyl in pharmaceutical dosage forms marketed in Australia.JPBA, 13(11),1355-1362.

[5] Mohamed, M. B.; Mohamed, E. E. and Arwa, M. I. 2015. spectrophotometric determinaton of Bisacodyl in pure form and tablet form. AJPAMC,3(1): 1-13.

[6] Basavaiah, K. and Somashekar, B. 2007. Quantitation of ranitidine in pharmaceuticals by titrimetry and spectrophotometry using dichromate as the oxidimetric reagent. J IranChem Soc,4(2): 78-88.

[7] Nief, R. and Nawal, A. M. 2011. Indirect spectrophotometric method for the determination of bisacodyl in commercial dosage forms and in environmenta l water samples. Iqr J Pharm,11(2): 77-81.

[8] Pamela, C. C.; Richard, F.; Michelle, A .C. and Luigi, X. C. 2006. Illustrated Reviews: Pharmacology, Lippincott Williams and Wilkins, Baltimor, 3rd Ed, PP 333.

[9] Barar, F. S. K. 2008. Essentials of Pharmacotherapeutics, New Delhi, 4th Ed, PP 539.

[10] Ramin, M. and Amir, A. 2006. Jouyban A. Amembrane Sensor for selective determination of bisacodyl in tablets. J Chin Chem Soc, 53(11):613-18.

[11] Mohamed, H.; Suzy, M.; Magda, H. and Tarek, S. 2004. Spectrophotometric determination of bisacodyl and piribedil. Anal. Lett.,37(2):247-262

[12] Fadia, H.; Abdelkawy, M. and Ibrahim, A. 2007. Development and validation of three stability indicating methods for determination of bisacodyl in pure form and pharmaceutical preparations. J AOAC int, 90(1):113-127.

[13] Laik, S. A. 1979. Determination of bisacodyl and its hydrolysis products in bisacodyl formulations by high preformance liquid chromatography. Fresenius Z. Anal Chem, 299 (83):124-126.

[14] Campbell, A. N. and Sherma, J. 2003. Development and validation of ahigh performance thin-layer chromatographic method densitometric detection for determination of bisacodyl in pharmaceutical tablets. Acta chromatographica, 13:109-16.

[15] Parandis, D.; Parvz, N. and Reza, G. M. 2009. Rapid determination of bisacodyl in flow-injection system combination by a novel sensitive square-ware voltammetry, Sensors and Actuators B: Chemical 136(1):66-72.

[16] Elvis, A. M. and Deepali, M. G. 2011. Development and validation of UV spectrophotometric method for determination of bisacodyl in suppositories. Int. J. Pharm Tech Res,3(1):193-196.

[17] Massaccesi, M. 1987. Chromatographic determination of two drugs: bisacodyl and sodium picosulphate. Ann. Chim. (Rome), 77:515–23

[18] Alaa, F.; Muneer, A. and Muhammad, H. 2012. Spectrophotometric determination of Levo-dopa in pharmaceutical preparation via oxidative coupling organic reaction. Kerbala Journal of
التقدير الطيفي لعقار البسكودايل في المادة النقية والمستحضرات الصيدلانية

اكتب اسمك أولاً:* اكتب اسمك الثاني:**

قسم الكيمياء، كلية التربية للعلوم الصرفة، جامعة ديالى، ديالى، العراق.
كلية الصيدلة، جامعة ميسان، ميسان، العراق.

الخلاصة:

يضمن البحث تطوير طريقة طيفية بسيطة ومضبوطة وحساسة لتقدير العقار بسكودايل في صيغته النقيّة وفي مستحضراته الصيدلانية. الطرقية المقترحة تعتمد على تفاعل ازدواج اللكوادل مع الكاشف اللوني داي نايترفويل في وجود بيرابودات الصوديوم ونتروكسيد الصوديوم كوسط قاعدي حيث يتكون مركب لونه أحمر يعطي أعظم امتصاص عند الطول الموجي 522 نانومتر. النتائج أظهرت مدى الخطأ بين التقدير والدليلا. السحبُيّة مقدارها (0.0555) مايكروغرام.سم١ ووحدة كشف نوعي للطريقة (0.0312) مايكروغرام.لمل وعامل ارتباط (0.9970) مع يزن مداها 2.00 مايكروغرام/مل وعامل امتصاص موالي مداها (0.6505) للثالوكسم 1 سم١ وسلامت (1.6). الطريقة طبقت بنجاح لتقدير البسكودايل في المستحضرات الدوائية وبنسبة استرجاعية أفضل من (99.16%).

الكلمات المفتاحية: التقدير الطيفي، عقار البسكودايل، المستحضرات الصيدلانية

مراجعات:

[1] Abdel-Hay, M. H.; Sabry, S. M.; Barary, M. H. and Belal, T. S. 2004. Spectrophotometric determination of bisacodyl and piribedil. Anal. Lett, 37:247–62.
[2] Ibrahim, A. 2011. Stability indicating analysis of bisacodyl by partial least squares regression, spectral residual augmented classical least squares and support vector regression chemometric models: A comparative study, Bulletin of Faculty of Pharmacy, Cairo University 49: 91–100.
[3] Basavaiah, K. 2007. Rapid titrimetric and spectrophotometric methods for salbutamol sulphate in pharmaceuticals using N-bromosuccinimide, Acta Pharm. 57: 87–98.
[4] Saadiyah, A.. 2011. New Azo Coupling Reactions for Visible Spectrophotometric Determination of Salbutamol in Bulk and Pharmaceutical Preparations. Dirasat, Pure Sciences, 38(2):153-160.