Indirect spectrophotometric method for the determination of bisacodyl in commercial dosage forms and in environmental water samples

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Received	Accepted
27.3.2011	3.7.2011

ABSTRACT

Objective: A simple, sensitive, and accurate indirect spectrophotometric method for the determination of bisacodyl in pure form and in some of its pharmaceutical preparations.

Method: The method is based on the oxidation of bisacodyl by iron (III), and subsequent complexation of iron (II) with o-phenanthroline.

Results: Forming a red-colored complex (ferroin) having the maximum absorbance at 510 nm. Beer's law is obeyed in the concentration range of 0.5-5 µg/ml. The molar absorptivity and sandell's sensitivity were 1.55×10^4 L.mol^{-1}.cm^{-1} and 0.0233µg.cm^{-2} respectively. The relative standard deviation (RSD) was less than 1.5 (n=11). The limits of detection and quantitation are 0.083 and 0.25 µg.ml^{-1} respectively.

Conclusion: The method is applied successfully for determination of bisacodyl in environmental water samples and in some pharmaceutical formulations (tablets and suppositories). A statistical comparison of these results with those of official method shows good agreement and indicates no significant difference in the precision.

الخلاصة

الهدف: وصف طريقة بسيطة وحساسة وذات دقة عالية لتقدير البسكودايل في حالته النقية وفي بعض مستحضراته الصيدلانية.

طريقة العمل: تعتمد الطريقة على أكسدة البسكودايل بواسطة الحديد الثلاثي حيث يكون ناتج التفاعل الحديد الثنائي والذي بدوره يتفاعل مع كاشف اورثوفينانثرولين (الفروين)

النتائج: تكوين معقد احمر اللون له اقصى امتصاص عند الطول الموجي ٥١٠ نانوميتر. وقد لوحظ ان قانون بيير يسري على الكميات التي تتراوح بين ٠.٥-٥ جزء بالمليون وبامتصاصية مولارية ١.٥٥ ×١٠^{٤} لتر.مول$^{-١}$.سم$^{-١}$ وبدلالة ساندل (دلالة الحساسية) ٠.٠٢٣٣ مايكروغرام\مل وان الانحراف القياسي النسبي للطريقة اقل من ١.٥% وان حد الكشف والحد الكمي كان ٠.٠٨٣ و٠.٢٥ مايكروغرام\مل على التوالي.

الاستنتاج: طبقت الطريقة بنجاح لتقدير البسكودايل في نماذج بيئية (نماذج مياه) وفي مستحضراته الدوائية (حبوب وتحاميل) كما اختبر نجاح الطريقة بمقارنتها مع الطريقة القياسية الدستورية المعتمدة باستخدام اختباري(F,t) عند حدود ثقة ٩٥% مما يدل على صلاحية التطبيق التحليلي للطريقة.

Bisacodyl is 4,4\` (pyrid - 2 – yl methylene) bis (phenyl acetate) [$C_{22}H_{19}NO_4$ =361.4] is a laxative used for the treatment of constipation, for evacuation of the colon before radiological examination of the abdomen, or endoscopy, and before or after surgical operations. It has little or no action on the small intestine. 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 given 5 milligrams by mouth or by rectum[1-4].

The literature survey reveals that only few methods have been reported for determination of Bisacodyl in pure form and in pharmaceutiacal formulations[5-11]. Official method includes potantiometric titration for pure form and UV spectrophotometric method for tablets and suppositories[5].

The spectrophotometric method include charge transfer and ion-pair complexation reaction[6]. Other methods reported for determination of bisacodyl like stability-indicating methods[7], high-performance liquid chromatography[8], high performance thin-layer chromatography[9], memberane sensor[10] and square-wave voltammetry[11]. The present work describes a new, simple indirect, spectrophotometric method for the determination of bisacodyl in pure form, pharmaceutical formulations and in water samplels. The method is based on the reaction of drug with ferric chloride and 1,10-phenanthroline at pH 3 resulting in the formation of ferroin, which absorbs maximally at 510 nm.

Experimental

Apparatus

Spectro-scan 50 UV- visible (double beam) spectrophotometer with 1.0 cm quartz cells was used for absorption measurements, and Jenway 3310 pH meter was used.

Reagents

All chemical used were of analytical or pharmaceutical grade and distilled water was used throughout.

Bisacodyl stock solution (Nineveh drug industry,NDI): 100 ppm, this solution was prepared by dissolving 0.01 g of pure bisacodyl in 100 ml 0.01 N HCl solution.

Bisacodyl standard solution (25 ppm) (6.9×10^{-5} M), this solution was prepared by diluting 25 ml of the stock solution to 100 ml by 0.01 N HCl in a volumetric flask.

Ferric chloride solution: 0.1 %, this solution was prepared by dissolving 0.1 g of ferric chloride in 100 ml distilled water containing 2 ml of concentrated HNO_3.

1,10-phenanthroline solution: 1%, this solution was prepared by dissolving 1 g of 1,10-phenanthroline in 10 ml of ethanol, then the volume completed to 100 ml with distilled water.

Buffer solution (pH3), this solution was prepared by mixing 16.2 ml of 0.1 M chloroacetic acid with 8.8 ml of 0.1 M KOH, then the volume was completed to 100 ml with distilled water in a volumetric flask[12].

Recommended procedure

A known volume of sample containing 12.5-125 μg of bisacodyl was transferred into a 25 ml calibrated flasks followed by addition of 1 ml of ferric chloride solution then 2 ml of buffer solution pH3 .The solution was mixed well and then heated in a water bath at 70 ± 2 ºC for 15 min. The content of each flask were cooled at room temperature and 5 ml of 1,10 phenanthroline solution was added. Finally the solution was diluted to the mark with distilled water, the absorbance of the red-colored products was measured at 510 nm against a reagent blank.

Analysis of pharmaceutical formulations

Ten tablets of bisacodyl were finely powdered and portion equivalent to 2.5 mg of bisacodyl was weighed accurately and stirred well with 3×10 ml portions of chloroform. The residue was filtered using whatman No.42 filter paper. The filtrate was evaporated to dryness and the residual drug was dissolved in 0.01 N HCl and transferred to a 100 ml standard volumetric flask which was then filled to volume with 0.01 N HCl. Treate 3 ml of this solution as mentioned under recommended procedure.

Weight five suppositories, transfer to a porcelin dish, melt and allow to cool while stirring with glass rod. Accurately weight a portion of the melted suppository mass, equivalent to

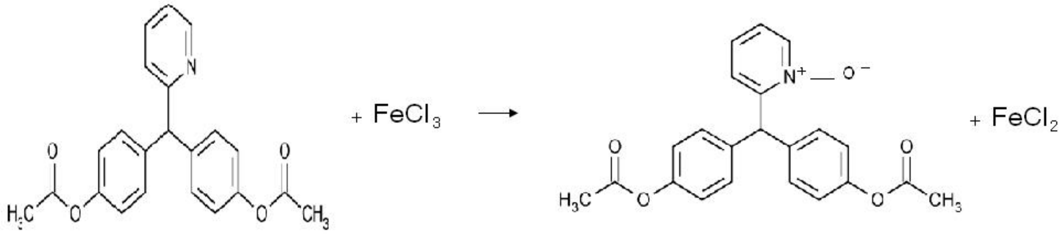
2.5 mg of bisacodyl, extract with 3×10 ml portions of hot 0.01 N HCl, cool and the residue was filtered. The filtrate was transferred to a 100 ml standard volumetric flask which was then filled to volume with 0.01 N HCl. Treate 3 ml of this solution as described under recommended procedure.

Environmental water samples

Distilled and tap water samples (100ml) were fortified with 2.5 mg of bisacodyl. The fortified water samples were analyzed as described under recommended procedure.

Results and discussion

The method is based on the oxidation of bisacodyl by iron III in presence of o-phenanthroline in acidic medium. The iron(II) formed was quantitively and rapidly converted to the stable tris (o-phenanthroline) iron II complex (ferroin) having an absorption maximum at 510 nm[13,14] as shown in Figure 1, thus permitting the indirect determination of bisacodyl.



$FeCl_2$+3 O -Phenanthroline $\longrightarrow$ Fe/ 3 O - Phenanthroline $+2Cl^-$
(red complex)

Figure 1. Oxidation of bisacodyl

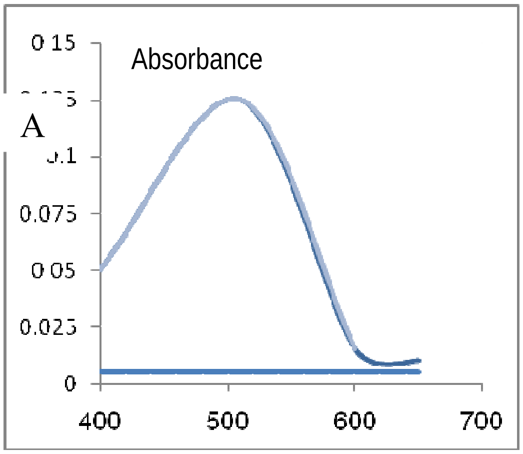


Figure 2. Absorbance spectra of A: bisacodyl. B: blank

Fig 2 Absorption spectra of A: 3µg /ml of bisacodyl with $FeCl_3$ and O-phenanthroline against reagent blank. B: blank against distilled water.The reaction variables were optimized by varying each variable while keeping other constants for obtaining maximum absorbance. The oxidation reaction was found to be quantitative in acidic medium, the pH 2.0-4.0 was considered optimum. Then, a pH of 3.0 was selected for the subsequent experiment. Four types of buffer solution pH3 of different composition15 have been tested for this purpose. Table [1] shows the results of this investigation.

1-3 ml of buffer B4 gave high sensitivity and 2 ml have been used for subsequent experiment. The effect of FeCl3 and o-phenanthroline amounts on the absorbance was investigated . A maximum and constant absorbance was found with 2 ml $FeCl_3$ and 5 ml of 1% o-phenanthroline, which were therefore adopted as being optimal. The color reaction occurred even at room temperature (25ºC), though at higher temperature the color developed more rapidly, the maximum absorbance was observed after 15 min of heating the solution at 70ºC. A stemperature of 70ºC and a reaction time of 15 min were selected for reproducible results. Under the experimental conditions described Beer's law is obeyed over the concentration range 0.5-5 $\mu g.ml^{-1}$ (Figure 3). Linear regression equation: A=0.01+0.04C(r=0.999 n=10), where A is the absorbance and C is concentration in µg/ml. The apparent molar absorptivity was 1.55×10^4 $l.mol^{-1}.cm^{-1}$ and sandell's sensitivity was 0.0233 $\mu g.cm^{-2}$. The limit of detection and quantification were evaluated as[16].

$$LOD = 3.3\,\frac{S_0}{b} \qquad LOQ = 3LOD$$

Where b is the slope and S_0 is the standard deviation of the regression line. The limit of detection was 0.083 $\mu g.ml^{-1}$ and the limit of quantification as the lowest standard concentration which could be determined with acceptable accuracy, and precision was 0.25 $\mu g.ml^{-1}$.

Table 1. Effect of different buffers on the absorbance

Ml of buffer solution	Absorbance			
	B_1	B_2	B_3	B_4
0.5	0.097	0.062	0.095	0.128
1	0.115	0.081	0.095	0.130
2	0.115	0.092	0.096	0.129
3	0.116	0.095	0.094	0.131
4	0.115	0.095	0.094	0.128
5	0.110	0.095	0.095	0.128

B_1: Buffer of 0.1 glycine – 0.2 M HCl, B_2: Buffer of 0.2 M KCl – 0.2 M HCl
B_3: Buffer of 0.1 M citric acid – 0.2 M Na_2HPO_4, B_4: Buffer of 0.1 M chloroacetic acid – 0.1 M KOH

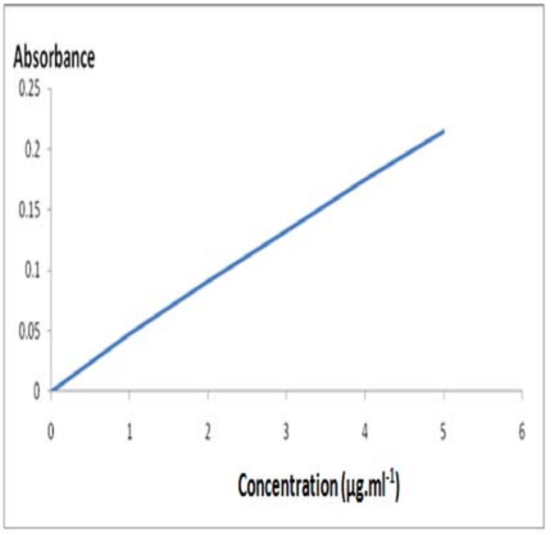


Figure 3. Calibration graph of bisacodyl

Table 2. Optical characteristics and statistical data for regression equation of the proposed method

Parameters	Value
λ max (nm)	510
pH	3.0
Beer's law limits (µg.ml^{-1})	0.5-5
Molar absorptivity (L.mol^{-1}.cm^{-1})	1.55×10^{4}
Limit of detection (µg.ml^{-1})	0.083
Limit of quantification (µg.ml^{-1})	0.25
Sandell's sensitivity (µg.cm^{-2})	0.0233
Correlation coefficient (r)	0.999
Regression equation (A=□+bc)	
Intercept (□)	0.01
Slope (b)	0.04
Recovery	100±0.89
Relative standard deviation (%)	< 1.5

Accuracy and precision

The accuracy and precision of the method were established by analyzing the pure drug solution at three different levels. The average recovery which is a measure of accuracy is 100 ±0.89% revealing high accuracy of the method. The relative standard deviation (RSD), which is an indicator of precision, was less than 1.5%, the result are complied in Table 2.

Interferences

A study of interference of some common excipients has been made during determination of 3.0 µg.ml^{-1} bisacodyl. It was observed that starch, glucose and lactose could be tolerated with a maximum amount of 12.0 mg, 20 mg and 55 mg respectively. However the drug content from powdered tablets was extracted with chloroform, which completely eliminates any interference by the common excipients found in drug formulations. Thus, the stability of the proposed method indicates that it can be used for the analysis of bisacodyl in drug formulations in the presence of various excipients found in the suppositories and tablets.

Application of the proposed method

The proposed method was successfully applied for the determination of bisacodyl in pharmaceutical formulations and environmental water samples.

Table 3 of the proposed method were compared with those of official method [5], using student t-test and variance ratio F-test at 95% confidence level. The calculated t and F values did not exceed the theoretical value indicting that there was no significant difference between the precision of the proposed and official method. It was also evident from the table that the results of bias (lower and upper limits) based on recovery experiments of the proposed method are acceptable (with the range of ± 2%).The Canadian health protection branch has recommended a bias of ± 2% (Q_L= 0.98 and Q_u= 1.02) in the pharmaceutical analysis, which was based on recovery experiment of the developed method[17] and the results of water samples Table 4 showed that the recovery values obtained were close to 100% .

Table 3. Determination of bisacodyl in pharmaceutical preparations

Pharmaceutical preparation	Amount of bisacodyl * Proposed method		official method		t value	F value
	Amount	recovery	Amount	recovery		
Bisacodyl tablets (5mg/tab)	5.03	100.6	4.97	99.4	1.63	1.54
Bisacodyl tablets (10mg/tab)	10.05	100.5	10.02	100.2	1.55	1.48
Bisacodyl suppositories (5mg\supp)	5.01	100.2	5.02	100.4	1.98	1.18
Bisacodyl suppositories (10 mg\supp)	10.05	100.5	10.08	100.5	1.88	1.26

* Mean of ten determinations.
T values (n=10, at 95% confidence level tabulated value 2.262).
F values (n1 and n2 =10, at 95% confidence tabulated value 3.18).

Table 4. Determination of bisacodyl in water samples

Water Samples	Added µg/ml	Found * µg/ml	Recovery %
Tap Water	0.3	0.302	101
	1.0	0.99	99.00
	2.5	2.47	98.88
Distilled Water	0.3	0.303	101
	1.0	0.98	98
	2.5	2.5	100

* mean value of six determinations

Table 5. Content uniformity testing of metformin hydrochloride tablets using the proposed method.

Parameter	% of the label claim
Tablet NO. 1	100.48
Tablet NO. 2	100.25
Tablet NO. 3	99.56
Tablet NO. 4	100.52
Tablet NO. 5	99.38
Tablet NO. 6	99.35
Tablet NO. 7	99.72
Tablet NO. 8	100.03
Tablet NO. 9	100.66
Tablet NO. 10	99.71
Mean ($\overline{x}$)	100.73
% RSD	0.54
Max. allowed unit[18]	±15%

Application of the method to content uniformity

The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in Table 5 indicates that the proposed method can accurately and precisely quantitates bisacodyl in its commercially available tablets. The mean percentage (with RSD) of the labeled claim found in ten tablets was (0.54%) which fall within the content uniformity limits specified by the USP 30[18].

Conclusion

The proposed method was simple, accurate, precise, sensitive and low economical cost. Furthermore, the proposed method doesn’t require elaboration of procedures, which are usually associated with chromatographic methods. The proposed method could be applied successfully for determination of bisacodyl in environmental water samples, pure form as well as in different dosage forms

References

1. The pharmaceutical codex, London, 1979, P.105.
2. parfitt K, Blake SC, Parsons PS, Martindale AV; The Extra pharmacopoeia; 32^{nd} edition, pharmaceutical press: London, 2005 p1251.
3. Rachmilewitz D, Karmeli F, Okon E. Effect of bisacodyl on CAMP and Prostaglandin E_2 content, (Na+k). ATP ase, adenyl clase, and phosphodiesterase activities of rat intestine. Dig Dis sci 1980;25(8) :602-607.
4. Remington: the science and practice of pharmacy, mack publisher company, Easton, pennsylvania 18042, 1995 volum 2 P.896.
5. British pharmacopiea, 2009, P. 724.
6. Mohamed H, Suzy M, Magda H, Tarek S, Spectrophotometric detemination of bisacodyl and piribedil. Analytical letters 2004;37(2):247-262
7. Fadia H, Abdelkawy M, Ibrahim A. Development and validation of three stability- indicating methods for determination of bisacodyl in pure form and pharmaceutical preparations. J AOAC int 2007;90 (1):113-127.
8. Laik SA. Detemination of bisacodyl and its hydrolysis products in bisacodyl formulations by high preformance liquid chromatography, Fresenius Z. Anal Chem 1979;299:124-126.
9. Campbell AN, Sherma J. Development and validation of a high performance thin-layer chromatographic method densitometric detection for determination of bisacodyl in pharmaceutical tablets. Acta chromatographica, 2003;13:109-16.
10. Ramin M, Amir A, Jouyban A. Amembrane Sensor for selective determination of bisacodyl in tablets. J Chin Chemi Soc 2006; 53:613-18.
11. Parandis D, Parvz N, Reza GM. Rapid determination of bisacodyl in flow-injection system combination by a novel sensitive square-ware voltammetry. 2009;136(1):66-72.
12. Zommer-Urbanska S, Bojarowicz H. Spectrophotometric investigation on protolytic equilibria of mefenamic acid and determination by means of Fe(III) in methanol-equeous media. J pharm Biomed Anal 1986;4:475-81.
13. MarezcenkoZ. Spectrophotometric determination of elements. Ellis worwood limited, chicheaster, 1976. p. 309-12.
14. Morrison RT, Boyed RN. s Organic chemistry. New York: Allyn and Bacon, INC, 3^{rd} edition, 1973, p. 1017.
15. Perrin DD, Dempsey B, Buffer for pH and metal ion control. London: Champan and Hall Ltd, 1974. p. 132-36
16. Basavaiah K, Somashekar BC. Quantitation of rantidine in pharmaceuticals by titrimetry and spectrophotometry using dichromate as the oxidimetric reagent. J Iran Chem Soc 2007;4: 78-88.
17. Canadian Health Protection Branch Gui deline-Acceptable method, Ministry of National Health and welfare. Canada Health protection Brand, Ottawa, Canada ,1992.
18. The United State Pharmacopeia Convection, Inc, 32 NF27, 2009, p. 382.