

Antidepressant drugs as novel spectrophotometric reagents for the determination of nano amounts of bromate in water and bread samples

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Abstract— Bromate has been determined by visible spectrophotometric method in nano level by using a class of antidepressant drugs namely imipramine hydrochloride (IPH), desipramine hydrochloride (DPH), clomipramine hydrochloride (CPH) and trimipramine hydrochloride (TPM) in presence 3-Methyl-2-benzothiazolinone hydrazone hydrochloride hydrate (MBTH) as electrophilic coupling reagent. The method involves the reduction of bromate by MBTH which then couples with the antidepressant drugs. The reaction was carried out at room temperature (27 °C) in acidic medium. The reaction produced a blue colour which gave maximum absorbance at 630 nm for MBTH-IPH/DPH/CPH/TPM method. The method obeys Beer's law in the range of 200-1400, 300-1200, 100-1200, 450-1500 ng mL⁻¹ for IPH, DPH, CPH and TPM, respectively. The intensity of the blue colour developed was stable for 24 hours. The molar absorptivity and Sandell's sensitivity gave different values with different reagents and the method was found to be very sensitive and reproducible. To determine the selectivity of the proposed method the salts of 11 cations and 8 anions were added to a recommended concentration of bromate solution and the results obtained were very satisfactory. The method was successfully applied for the determination of bromate in water samples collected from different sources and wheat/bread samples obtained from commercial factories.

Keywords— Bromate, Dibenzazepines, Spectrophotometry, Water, Bread, IPH, DPH, CPH, TPM

I. INTRODUCTION

Water treatment is an important process in the present-day context due to the high surge of industrial effluents and increasing level of water pollution. When water treatment is considered, chlorination is a popular method but ozonization has proved to be a best alternative [1]. The water treatment process of chlorination produces trihalomethanes which cause health related problems [1,2].

In natural water, bromate content is absent, but during ozonization it is a by-product of bromide produced in water. During the disinfection process of drinking water which contains bromide and bromide containing compounds using ozone, bromate is a by-product obtained during the treatment. When drinking water comes in contact with the source water in the soil containing bromide or the sea water which has high bromide content the bromide present in the water from the soil is converted into carcinogenic bromate during ozonization treatment of drinking water and waste water treatment plants [3] and the chances of the bromate content is higher when calcium chloride is used along with ozone. Depending on the source of water samples the level of bromide may vary and it will be higher or lower depending on the environmental conditions and where it is found. The content of bromide in water samples fluctuate to lower and higher levels as an effect of other factors also like the contact period of the ozone with the water sample and factors related to water chemistry including pH, organic material, hardness and alkalinity.

As bromate is found to be a potential human carcinogenic agent, the distribution of water for drinking and household purposes should be carefully checked up by the public water bodies to ensure the correct amount of bromate present in it. The reported concentration level of bromate in ozonated water is 60-90 µg L⁻¹ [4,5].

The presence of bromate in the water samples can be eliminated using three different processes, the first method is the removal of bromide before the water sample is subjected to ozonization: second is to have a control on the amount of bromate formation during ozonization and third is the removal of bromate from the water sample after ozonization. In some of the water samples where the concentration of bromide is greater than 50 µg/L, it is recommendable to use control measures like decrease in pH or with the addition of ammonia for a lesser rate of bromate formation. [6]

In the bread making process, the tendency of fresh milled wheat flour to produce bread is high initially which starts to decrease gradually and in about two to three months it deteriorates completely. In order to increase the shelf life of the wheat flour in the bread making process flour improvers are added during the manufacture. When flour improvers are considered, potassium bromate is the best [7]. The international Agency of Research Cancer (IARC) has classified bromate in Group 2B as a primary cancer-causing agent. Because of this carcinogenic effect of bromate it is indeed very important to rule out the presence of potassium bromate in the bread. Bromate has both positive and negative effects in day-to-day life and hence maintaining a balanced level of it is of paramount significance in drinking water and the foods which are consumed by humans. Also, the importance of bromate provokes a need for developing methods for its determination. The methods which are available in the literature for the determination of bromate consists of chromatographic [8 -15], electrochemical [16-19] and optical methods [20-26]. Visible spectrophotometric methods are the most appropriate when optical methods are considered as they are simple and cost effective when compared to other instrumental methods. Besides, visible spectrophotometric detection is much more viable as a useful technique to develop on-line or at-line systems.

When the literature studies on the determination of bromate ions in different samples is accounted, it has been noticed that the visible spectrophotometric determination methods are limited and these are mainly based on its oxidation property to give different products. These methods include: reduction of bromate with sodium nitrite [27], reaction with 3,5-dibromo-PADAP and thiocyanate in a strong acidic medium [28,29], oxidation of 1,2,4-trihydroxyanthraquinone-3- carboxylic acid in an acidic medium, producing a change in colour [30] and oxidation of phenothiazines to yield radical cation coloured product [31]. But these reported methods have their own limitations when the sensitivity and stability is taken into account. The determination of bromate in nano level was not reported in any of the above-mentioned methods and the colour produced during the determination was not stable [28].

In this paper a new class of analytical reagents have been proposed which involves N-substituted dibenzazepines. Antidepressant drugs namely imipramine hydrochloride (IPH), desipramine hydrochloride (DPH), clomipramine hydrochloride (CPH) and trimipramine hydrochloride (TPM) are used for the spectrophotometric determination of

bromate in nano levels by using an electrophilic coupling reagent 3-Methyl-2-benzothiazolinone hydrazone hydrochloride hydrate (MBTH) as electrophilic coupling reagent to produce a blue colour. The procedure was satisfactorily applied for the bromate determination in water samples collected from different sources and wheat/ bread samples. The obtained results were compared with the existing methods which used different chromogens and the procedure developed here offered many advantages with respect to simplicity and sensitivity.

II. MATERIALS AND METHODS

UV-VIS spectrophotometer UVIDEC-610 type with 1.0-cm matched was used throughout the determination to measure the absorbance values of the blue colour complex obtained.

Potassium bromate was used to prepare the standard solution of bromate. A stock solution of

1000 $\mu\text{g mL}^{-1}$ of bromate was prepared by dissolving known quantities of potassium bromate in 1 litre of distilled water. This stock solution was further diluted with distilled water to get the required strength solutions used in the determination. An aqueous solution of MBTH (0.05% w/v) was prepared by dissolving 50 mg of the compound in 100 mL of distilled water. Due to the sensitivity of MBTH solution to sunlight it is preferred to store the solutions in amber bottles.

Solutions of IPH, DPH, CPH and TPM (0.05% w/v) were prepared in distilled water. Solutions of diverse ions required to study the inference effect were prepared by dissolving the respective salts in water. All other chemicals used were of analar grade.

Procedures

A series of 25-mL standard flasks were used in which different volumes of standard solution of bromate was added. To each flask, 2.0 mL of 2N (v/v) hydrochloric acid, 1.0 mL of MBTH (0.05% w/v) and 3.0 mL of IPH, DPH, CPH or TPM (0.05% w/v) were added. The contents in the standard flask were shaken well and the flasks were set aside undisturbed for about 10 min. After the formation of the blue colour the solutions were made up to mark using distilled water. The absorbance for the blue colour solutions obtained were recorded with reference to corresponding reagent blank obtained in the similar manner without the addition of bromate solution. Table 1 gives a detailed observation of the optical characteristics using IPH, DPH, CPH and TPM for the determination of bromate.

Table 1: Observed parameters for bromate determination with IPH, DPH, CPH and TPM

Parameters	IPH	DPH	CPH	TPM
Beer's law (ng mL ⁻¹)	200-1400	300-1200	100-1200	450-1500
Recommended drug concentration (ng mL ⁻¹)	500	500	500	500
Molar absorptivity (L mol ⁻¹ cm ⁻¹)	5.68x10 ⁴	5.97x10 ⁴	3.50x10 ⁴	0.98x10 ⁴
Sandell's sensitivity (ng cm ⁻²)	4.0	2.0	10.0	1.8
Regression equation*				
Slope (a)	0.3938	0.5000	0.2829	0.5111
Intercept (b)	0.0302	-0.0002	0.0418	0.0187
Correlation coefficient	0.9969	0.9988	0.9893	0.9999
R.S.D**	±1.07	±0.62	±0.87	±1.02

*y=ax+b where x is the concentration of bromate in ng mL⁻¹

** relative standard deviation(n=5)

The blue colour developed in the method showed a maximum absorption (λ_{max}) at 630 nm and it was found to stable for 24 hours.

III. RESULTS AND DISCUSSION

For the treatment of depressive disorders [32], the commonly used drugs are tricyclic antidepressants and their efficiency in the treatment of depression has been confirmed. When the other alternatives fail in the treatment of depression IPH and DPH are used when hysterical traits are present. There is an acute impact by CPH on electrophysiological features of sleep and anxiolytic activity is observed to be exerted by TPM.

When the uses of dibenzepines are taken into account their applications are not only in pharmaceutical but it has been observed that two of the benchmark antidepressant agents (IPH, DPH) have also been used as reagents for the detection of micro amounts of blood in faeces[33] and urine[34].

The electrophilic coupling reagent 3-Methyl-2-benzothiazolinone hydrazone hydrochloride hydrate was developed for the first time in the determination of aromatic amines, imino heteroatomic compounds and aliphatic aldehydes. After this it was successfully used for the determination of a large number of organic compounds such as those containing methylene groups, carbonyl compounds, Schiff's bases, aromatic hydrocarbons, saccharides, steroids, olefins, phenols, furfural and heterocyclic bases [35].

Reaction Mechanism

The spectrophotometric determination of bromate involves a chemical reaction in which it is reduced by the electrophilic coupling reagent MBTH and the reduced form couples with antidepressant drugs IPH, DPH, CPH and

TPM to produce a blue colour complex in an acidic medium. The blue colour was found to have a maximum absorption at 630 nm. The colour development was carried out at room temperature (27 °C) and the intensity of the blue colour was found to be stable for 24 hours. The factors affecting the colour development, sensitivity and adherence to Beer's law were investigated as according to the standard procedure and the results showed that the method is quite sensitive and reproducible for the determination of bromate in nano level.

Optimization of analytical variables

In order to develop a standard procedure for the proposed method the concentration and the quantity of the reagents needed for the development of the blue colour with a maximum intensity was studied. A particular parameter was optimized by fixing the remaining parameters as a constant. For example, when the concentration and volume of bromate, MBTH and acid is fixed; it was observed that the colour intensity was maximum when 2.0-5.0 mL of 0.05% (w/v) of IPH/DPH/CPH/TPM solution were taken. Hence, during the determination, 3.0 mL of 0.05% (w/v) IPH/DPH/CPH/TPM were used for routine analysis. To fix the amount of MBTH and acid the above procedure was repeated to get the maximum intensity of the blue colour. Similar experiments were conducted to fix the amount of MBTH and acid required to get same intensity of colour every time. It was observed that for reproducible results 1.0 mL of 0.05% (w/v) MBTH solution and 2.0 mL of 2N HCl (v/v) solution should be used.

Order of addition

The order of the addition of the reactants is also an important parameter in the development of coloured products in spectrophotometric determinations. During the procedure the addition of bromate, MBTH, dibenzazepine and acid was studied through the formation of the blue-coloured product. But the sequence of addition of the reactants did not alter the intensity of the colour and no appreciable change in colour development was observed.

Temperature and stability

It was observed that during the chemical reaction the development of the colour decreased as the temperature was increased above the room temperature (27 °C). Hence the development of the blue colour was carried out at room temperature (27 °C). The intensity of the blue colour developed was stable for 24 hours.

Analytical Parameters

The blue-coloured product with maximum absorption at 630 nm obeyed Beer's law in the range of 200-1400, 300-

1200, 100-1200, 450-1500 ng mL⁻¹ for IPH, DPH, CPH and TPM, respectively. The optical parameters as required for the spectrophotometric studies such as optimum range for the determination of the ions as evaluated from a Rigbom plot, molar absorptivity, Sandell's sensitivity, slope, intercept, correlation co-efficient were calculated as per the standard procedure and the results are tabulated in Table 1. The results indicate that the method is sensitive.

Selectivity

The selectivity of MBTH-IPH/ DPH method was determined by studying the effect by adding 100mg of the salts of 11 cations and 8 anions. During the inference studies 500 ng mL⁻¹ of bromate was used and satisfactory results were obtained with an acceptable error of ±3%. The error obtained during the studies was tolerable which indicated that the proposed method can be employed for the determination of bromate without the interference of the ions even when they present in 160-fold excess over the bromate concentrations. The results presented in Table 2 and 3 indicate that the method is highly selective.

Table 2: Effect of cation on the determination of bromate in the visible region. MBTH-IPH/DPH method medium, acidic; bromate-500 ng mL⁻¹; 2N HCl, 2 mL; 0.05%MBTH,

1 mL, 1 mL and 0.05% IPH/DPH, 3 mL: λ_{max} 630 nm

Salt of the cation added	Amount added mg	% Recovery of ion* ± RSD**	
		IPH	DPH
Aluminium ammonium sulphate	100	99.4 ± 0.65	99.8 ± 0.70
Ammonium molybdate	100	98.6 ± 1.04	98.2 ± 1.02
Barium chloride	100	99.6 ± 0.79	98.7 ± 1.02
Cadmium sulphate	100	99.6 ± 0.98	98.8 ± 0.82
Lead nitrate	100	99.4 ± 1.03	100.4 ± 0.96
Magnesium carbonate	100	100.6 ± 1.09	99.6 ± 0.76
Selenium sulphate	100	98.7 ± 0.86	98.8 ± 0.82
Sodium arsenate	100	98.4 ± 0.68	99.8 ± 0.53
Strontium nitrate	100	98.2 ± 0.52	99.4 ± 0.79
Tin chloride	100	99.6 ± 0.84	99.6 ± 1.06
Zinc chloride	100	98.6 ± 0.62	99.3 ± 0.83

*500 ng mL⁻¹ of bromate taken

** relative standard deviation(n=5)

Table 3: Effect of anion on the determination of bromate in the visible region

Salt of the cation added	Amount added mg	% Recovery of ion* ± RSD**	
		IPH	DPH
Ammonium chloride	100	98.6 ± 0.67	98.7 ± 1.02
Potassium tartarate	100	99.4 ± 0.97	98.2 ± 1.02

Potassium sulphate	100	99.6 ± 0.79	100.4 ± 0.96
Sodium chloride	100	98.7 ± 0.86	98.8 ± 0.82
Sodium carbonate	100	99.4 ± 1.03	99.6 ± 0.76
Sodium sulphate	100	100.6 ± 1.09	99.8 ± 0.53
Sodium phosphate	100	99.6 ± 0.98	98.8 ± 0.82
Sodium bicarbonate	100	98.4 ± 0.68	99.8 ± 0.70

*500 ng mL⁻¹ of bromate taken

** relative standard deviation(n=5)

Applications

(i) Bromate in water samples:

Water samples from four different nearby available samples were collected and the method (MBTH-IPH/DPH) was applied to assess the validity by adding known amounts of

bromate to the collected samples. The results detailed in Table 4 clearly indicated that the method is well suited for the routine analysis of bromate determination in water samples. An error of ±2 % was obtained which is in well acceptable range.

Table 4: Bromate in water samples (MBTH-IPH/DPH method)

Sample	Bromate ng mL ⁻¹			Recovery by ± RSD**	
	Added	Recovered by proposed method		IPH	DPH
		IPH	DPH		
Tap water	300	295	297	98.3±0.92	99.0±0.86
	400	409	407	102.2±1.04	101.8±1.02
	500	503	504	100.6±0.78	100.8±0.80
Borewell water	300	294	295	98.0±1.12	98.3±0.92
	400	393	394	98.3±0.74	98.3±1.08
	500	496	498	99.2±0.90	98.5±0.82
Lake water	300	292	296	97.3±1.02	98.6±1.08
	400	387	402	96.8±0.60	100.5±0.76
	500	487	498	97.4±0.88	99.2±0.92
Ozonated water*	300	296	302	98.6±0.72	100.6±0.86
	400	404	396	101.0±1.08	99.0±1.12
	500	506	502	101.2±0.68	100.4±0.72

*samples were free from ozone at the time of determination

** relative standard deviation

(ii) Bromate in unblended flour and bread:

Different factories from the nearby surroundings were considered to determine the percentage of bromate recovered in untreated and unblended wheat flour and the proposed procedure (MBTH-IPH/DPH) was applied. About 5.0 g of the wheat flour from different factories was taken and 25 mL of water and varying amounts of potassium bromate were added and the contents were shaken well in order to obtain a uniform mixture. The contents were then

extracted ultrasonically at room temperature for about 10 minutes after which it was subjected to centrifugal separation. This process led to the formation of two layers, the supernatant was filtered and percentage recovery of bromate was determined directly using the proposed method. The results given in Table 5 indicate that the methods can be satisfactorily applied for commercial samples.

For the analysis of bromate present in commercial bread samples, a 15mm thick and 2 cm diameter circular sample of a bread slice was taken. The sample of the bread slice was frozen and dried under vacuum for 48 hours and then was powdered to a fine course. A portion of the powder (2 grams) was weighed and transferred to a beaker. To this 20 mL of distilled water was added and the mixture was subjected to ultrasonic extraction at room

temperature(27°C) for 10 min followed by centrifugal separation. The liquid fraction of the subjected mixture was separated, filtered and diluted with distilled water to 100 mL mark. Suitable aliquots of this solution were taken and the proposed procedure (MBTH-IPH/DPH) method was employed. The results tabulated in Table 5 gives the percentage recoveries which indicates clearly that the method is reliable.

Table 5: Bromate in flour and bread samples (MBTH-IPH/DPH method)

Sample	Bromate added in ng mL ⁻¹	Bromate found * in ng mL ⁻¹		Recovery by ± RSD**	
		IPH	DPH	IPH	DPH
Flour [#]	-	32.10	31.66	100.8±0.67	98.5±0.56
	30.00	61.44	62.44	99.3±1.02	97.4±0.90
Flour [#]	-	31.66	32.22	96.8±0.60	99.5±0.98
	40.00	73.45	72.66	100.1±0.90	98.5±0.81
Flour [#]	-	34.12	35.62	99.7±0.81	100.3±0.70
	50.00	82.06	84.78	100.1±0.60	100.8±0.42
Bread	-	616	620	102.2±1.04	99.0±0.86
	300	921	918	98.0±1.12	100.6±0.78
Bread	-	624	620	101.0±1.08	98.6±1.06
	400	1020	1022	100.6±0.78	100.8±0.80
Bread	-	604	607	99.0±1.12	98.3±0.92
	500	1108	1105	97.4±0.88	99.2±0.92

*average of three determinations

** relative standard deviation

#expressed as µg g⁻¹

IV. CONCLUSION

As the visible spectrophotometric methods for the determination of bromate is indeed of great importance, it may be concluded that the proposed method which involves imipramine hydrochloride (IPH), desipramine hydrochloride (DPH), clomipramine hydrochloride (CPH) and trimipramine hydrochloride (TPM) for the determination of bromate in water and wheat/ bread samples is highly sensitive and has good reproducibility. 3-Methyl-2-benzothiazolinone hydrazone hydrochloride hydrate (MBTH) is used as electrophilic coupling reagent in the method to give the blue colour complex. The use of common reagents and also the aqueous medium makes the methods cost-effective and versatile. In summary, among the four spectrophotometric reagents IPH, DPH, CPH and TPM, we recommend IPH or DPH for routine analysis in industries and laboratories.

REFERENCES

- [1] Siddiqui M.S., Amy G. L., Murphy B.D. Ozone enhanced removal of natural organic matter from drinking water source, *Water Res* 1997; 31,3098-3106.
- [2] Bull R.J., Kopley F.C., Health effects of Disinfectants and Disinfection By-Products 1991 AWWARF and AWWA, Denver Co.
- [3] Kurokawa Y., Takayama S., Konishi Y., Hiasa, Y., Asahina, S., Takahashi M., Maekawa A., Hayashi, Y. Long-term in vivo carcinogenicity test of potassium bromate, sodium hypochlorite and sodium potassium bromate, sodium hypochlorite and sodium chlorite conducted in Japan, *Environ. Health Perspect* 1986;69, 221-235.
- [4] Haag W.R., Holgne J. Ozonation of bromide-containing water: Kinetics of formation of hypobromous acid and bromate, *Environ.Sci.Technol* 1983; 17, 261-267.

- [5] McGuire M.J., Krasner S.W., Gramith J.T. Comments on bromide levels in state project Water and Impacts on control of Disinfectant By-Product, Metropolitan water District of Southern California: Los Angeles, C.A.1990.
- [6] Urs Von Gunten. Ozonation of drinking water: Part II. Disinfection and by-product formation in presence of bromide, iodide or chlorine, Water Research 2003;37, 1469-1481.
- [7] Dennis M.J., Burrell A., Mathieson K., Willets P., Massey R.C. The determination of the flour improver potassium bromate in bread by gas chromatographic and ICP-MS methods, Food Addit Contamin 1994;11, 633-639.
- [8] Achilli M., Romele L. Ion chromatographic determination of bromate in drinking water by post-column reaction with fuchsin, J Chromatogr A, 1999; 847, 271-277.
- [9] Arnaud D., Spiros P.A. Ion chromatography in series with conductivity detection and inductively coupled plasma-mass spectrophotometry for the determination of nine halogen, metalloids and non-metal species in drinking water, J Anal Atomic Spectrometry, 2001; (16) 575-580.
- [10] Bichsel Y., Gunten U.V. Determination of iodide and iodate by ion chromatography with post column reaction and UV/visible detection, Anal Chem, 1999; (71) 34-38.
- [11] Hu W., Takeuchi T., Haraguchi H. Electrostatic ion chromatography, Anal Chem, 1993; (65) 2204-2208.
- [12] Kumar S.D., Maiti B., Mathur P.K. Determination of iodate and sulphate in iodized common salt by ion chromatography with conductivity detection, Talanta, 2003; (53) 701-705.
- [13] Liu Y., Mou S. Determination of bromate and chlorinated haloacetic acids in bottled drinking water with chromatographic methods, Chemosphere, 2004; (55) 1253-1258.
- [14] Liu Y., Mou S., Heberling S. Determination of trace level bromate and perchlorate in drinking water by ion chromatography with an evaporative preconcentration technique, J Chromatogr A, 2002; (956) 85-91.
- [15] Mohammed A., Tiwari S., Singh J.P.C. Thin-layer chromatographic separation, identification and determination of certain anions, J. Chromatogr Sci, 1995; (33) 143-147.
- [16] Jakmnee J., Grudpan K. Flow injection amperometry for the determination of iodine in iodized edible salt, Anal Chim Acta, 2001; (438) 299-304.
- [17] Takayanagi K., Wong G.T.F. The oxidation of iodide to iodate for the polarographic determination of total iodine in natural waters, Talanta, 1986; (33) 451-454.
- [18] Wong G.T.F., and Zhang I.S. Chemical removal of oxygen with sulfite for the polarographic or voltammetric determination of iodate or iodide in sea-water, Mar. Chem, 1992(1) 109-116.
- [19] Yasypchuk B., Novotny I. Determination of iodates using silver solid amalgam electrodes. Electroanal, 2002; (14) 1138-1142.
- [20] Chakraborty D., Das A. D. Indirect determination of iodate by atomic absorption spectrophotometry, Talanta, 1989; (36) 669-671.
- [21] Gong B.L., Gong G. Q., Wang H.C. A fluorescence quenching method for the determination of iodate ion with fluorescein, Fenxi Hauxue, 1997; (25) 906-908.
- [22] Kamson O.F. Spectrophotometric determination of iodate, iodide and acids by flow-injection analysis, Anal Chim Acta, 1986; (179) 475-479.
- [23] Mendez J.H., Mateos A.A., Parra A.M.J., de-Maria C.G., "Iodometric flow-injection determination of traces of oxidants. Determination of iodate and active chlorine," Quim. Anal., 6(1987) 60-67.
- [24] Oguma K., Kitada K., Kuroda R. Microchemical determination of iodate and iodide in sea-waters by flow-injection analysis, Mikrochim Acta, 1993; (110) 71-77.
- [25] Zhao X.C., Kou Z.X., Hu Z. Determination of iodate by flow-injection analysis with 5-Br-PADAP[2-(5-bromo-2-pyridylazo)-5-diethylamino-o-phenol] and thiocyanate, Mikrochim Acta, 1991; (1) 279-283.
- [26] Zui O.V., Terletskya A. V. Rapid chemiluminescence method for the determination of iodine traces, Fresenius J Anal Chem, 1995; (351) 212-215.
- [27] Robert C. D., Jesse S.W. Determination of bromate and chlorate via reduction with sodium nitrite, Analyst, 1994; (119) 2141-2143.
- [28] Ketai W., Huitao L, Jain H., Xingguo C. Zhide H. Determination of bromate in bread additives and flours by flow injection analysis, Food Chem, 2000(70) 509-514
- [29] Staden J.F.V., Mulaudzi L.V., Stefan R.I. Spectrophotometric determination of bromate by sequential injection analysis, Talanta, 2004; (64) 1196-1202.
- [30] Salinas F., de la Pena A. M., Murillo J.A. Spectrophotometric determination of BrO_3^- by oxidation of 1,2,4-trihydroxyanthraquinone-3-carboxylic acid, Mikrochim Acta, 1984; (11) 75-83.
- [31] Farrell S., Jos J.F., Pacey G.E. Spectrophotometric determination of bromate ions using phenothiazines, Anal Chim Acta, 1995; (313) 121-129.
- [32] Wilson and Gisvold, "Textbook of Organic and Pharmaceutical chemistry," Ed., Doerge R.F. 8th edition, Lippincott, Philadelphia, 1982.

- [33] Syed A.A., Khatoon B.A., Silwadi M.F. New reagents for detection of feecal occult blood, *J Pharm. Biomed. Anal*, 2001; (24) 581-586.
- [34] Syed A.A., Silwadi M.F., Khatoon B.A. Imipramine hydrochloride and desipramine hydrochloride as new reagents for detection of microamounts of blood in urine *J Pharm. Biomed. Anal*, 2002;(28) 501-507.
- [35] Pospisilova M., Polasek M., Svobodova D. Spectrophotometric study of reactions of substituted phenols with MBTH in alkaline medium: The effect of phenol structure on the formation of analytically useful coloured products, *Mikrochim. Acta*, 1998; (129) 201-208.