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Potentiometric Determination of Imatinib under Batch and Flow Injection Analysis Conditions

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A new potentiometric electrochemical sensor (ion-selective electrode) based on the formation of ion associate of Imatinib mesylate with sodium tetraphenyl borate in polyvinyl chloride plactisized with dioctylphythalate was developed .Such electrode was prepared for the assay of the cited drug in its pure form and pharmaceutical formulations under batch and flow injection analysis conditions. The life span of the electrode is 30 days on continuous soaking and several months when kept in dry conditions. It is characterized by usable concentration range of (1.0×10^{-5}-1.0×10^{-3} M) and (5.0×10^{-6}-1.0×10^{-2} M) in batch and FIA conditions, respectively. The change of pH does not affect the potential reading or peak heights of the electrode in the range of 4.00-7.50 in batch condition. While in FIA, the peak heights representing the pH are almost stable in the range 4.00-6.00. The electrode is highly selective towards many inorganic cations, and neutral molecules. The obtained results indicated high accuracy and precision of the studied electrode as sensor for the drug.

Keywords: Imatinib, FIA, Potentiometric Determination, Ion-Selective Electrode, Imatinib Mesylate

1. INTRODUCTION

Imatinib mesylate methanesulfonic acid; 4-[(4-methylpiperazin-1-yl)methyl]-N-[4-methyl-3-[(4-pyridin-3-ylpyrimidin-2-yl)amino]phenyl] benzamide, is a tyrosine kinase inhibitor [1], that was found to be one of the most recent medications used for the treatment of chronic myeloid leukemia and gastro-intestinal stromal tumor. The introduction of Imatinib mesylate, which targets the kinases presenting with these molecular alterations, has dramatically changed the management of these rare tumors, which were resistant to conventional cytotoxic chemotherapy, both in advanced and localized phases [2]. It has opened a new area in cancer therapy and is given orally and chronically, that is why

it was chosen as a model drug [3]. It is also known as Signal Transduction Inhibitor 571 and as antineoplastic agent. Its target protein is produced by DNA translocation (Philadelphia chromosome), which leads to a fusion protein of Abl with Bcr termed Bcr-Abl [4].

Many methods were reported in literature for the determination of imatinib mesylate in bulk, dosage forms and biological fluids, although it is not official in any pharmacopeia some of these methods are HPLC/UV detection [5-9], HPLC/Mass detection [10-14], gas chromatography [15, 16], supercritical fluid chromatography [17], capillary electrophoresis [18, 19], voltammetric methods [20, 21] and spectrophotometric methods [22, 23].

The aim of this work is to develop a new ion-selective membrane electrode based on the ion-exchanger imatinib tetraphenyl borate used in the analysis of the drug in its pure and pharmaceutical formulation, Gleevec® capsules (100mg/capsule) under batch and flow injection analysis (FIA) conditions. The proposed method is simple and suitable for determination of the drug providing economic, less time consuming and more sensitive procedure compared with the reported spectrophotometric method (reference method) [22].

2. EXPERIMENTAL

2.1. Apparatus

Measurements under batch were carried out using pH-meter Jenway 3510 (England) and potentiometer (Schott tritroline TA 10 plus, Germany). The temperature of the test solutions was controlled using a thermostat (Lauda, Germany). Packed saturated Calomel (Sentek, UK) was used as an external reference electrode.

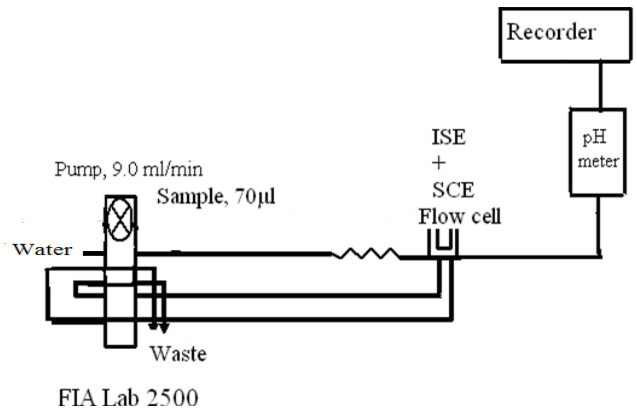

Figure 1. Schematic diagram of the flow injection system used in the measurements.

Measurements under FIA were performed using flow injection analysis (FIA lab 2500, USA) which included 4 channels peristaltic pump, 6 port -2 way injection valve connected to Jenway 3510 pH–meter and interfaced to strip–chart recorder model BD111 from Kipp and Zonn (Deft, Netherlands). A wall-jet-cell, providing low dead volume, fast response, good wash characteristics,

ease of construction and compatibility with electrodes of various shapes and sizes, was used in flow determinations where a Perspex cup with axially positioned inlet polypropylene tubing is mounted at the sensing surface of the electrode body [24, 25]. The optimized distance between nozzle and the sensing surface of the electrode was 5 mm; this provides the minimum thickness of the diffusion layer and consequently fast response. The ion-selective electrode with flow cup, reference electrode and the outlet tube were placed in a beaker, where the level of solution was kept 1 cm above the electrode surface. The FIA system used is represented in Figure 1.

2.2. Materials and reagents

All chemicals and reagents used were of analytical grade. Doubly distilled water was used. Solvents were of HPLC or spectroscopic grade. Imatinib mesylate was provided by Novartis (Basel, Switzerland) and Hangzhou Hetd Industry Co, Ltd (China). Gleevec® capsules (each containing 100 mg imatinib mesylate) provided by Novartis. Methanol and Methylene chloride were provided by El Goumhouria Company for Trading, Medicines, Chemicals and Medical Appliances. Sodium tetraphenyl borate ($C_{24}H_{20}BNa$), Fluka, Polyvinyl chloride (PVC) (Fluka), of high relative molecular weight, plasticized with Dioctylphthalate (DOP) [$C_{24}H_{38}O_4$] (Fluka) was used for preparing membranes. In FIA measurements, doubly distilled water was used for preparing solutions and as a flow stream. The carrier and reagent solutions were degassed by means of vaccum-suction and sample solutions were freshly prepared prior to measurements.

2.3. Factors affecting the performance characteristics of the electrode

Stock concentrated solution ($1.0x10^{-2}$ M) of the drug was prepared by dissolving the accurately weighted amount of the drug in water. Lower concentrations were prepared by appropriate dilutions. The stock solution and dilutions were kept in volumetric flasks in the refrigerator. The ion-exchanger imatinib tetraphenyl borate was prepared by the addition of 50 mL of $1.0x10^{-2}$ M imatinib mesylate solution to 50 mL of $1.0x10^{-2}$ M of sodium tetraphenyl borate. The developed precipitate was left overnight to assure complete coagulation, filtered and washed several times with distilled water, and left to dry at room temperature for at least 48 hrs. Membranes of different compositions were prepared by mixing the required amounts of ion-exchangers, PVC and plasticizer (DOP) of total weight 0.35 g in a 5.0 cm (diameter) Petri-dish containing 7 mL tetrahydrofuran and 3 mL acetone. To obtain homogeneous and uniform thickness, the amount of solvent was kept constant and the membranes were left covered to dry in air (not less than 48 hr) [26, 27]. The conditions of optimization of the electrode response under batch conditions in terms of usable concentration range, effect of soaking, effect of pH of the test solution and effect of interfering ions as a mean of evaluation of the electrode selectivity were optimized. The separate solution method [SSM] [28] was applied for inorganic cations and matched potential method [MPM] [29] was applied for neutral molecules as sugars and urea.

For the optimization of the FIA response, several parameters should be tested and optimized such as sample volume where samples of different volumes (70-230 μL) were injected, effect of flow

rate (5.00-10.00 mL/min.), effect of carrier composition and dispersion coefficient measurements. The effect of pH of the test solution on the electrode potential was studied by preparing a series of solutions with concentrations $1.0x10^{-2}$ M of the drug having different pH values ranging from pH 1.00-12.00 which were then injected in the flow stream, and their peak heights were compared with each other. The electrode selectivity was studied using a series of standard imatinib solutions of concentrations $5.0x10^{-6}$-$1.0x10^{-2}$ M was prepared, its corresponding peak heights were measured and then solutions with concentration $1.0x10^{-2}$ M of interferents were measured under the same conditions. The peak heights were converted to millivolt, compared to those obtained from the standard drug series and then used for calculating the selectivity coefficient of the electrode towards these ions or molecules using the matched potential method [MPM] [29].

2.4. Analytical applications

Standard additions methods [30] in batch measurement and peak height comparison under FIA conditions were applied.

The developed electrode has been used for the determination of imatinib mesylate in its pure form and its pharmaceutical preparation (Gleevec® 100mg/capsule) by applying standard additions method under batch conditions, in which a known change in concentration is made through the addition of constant increments of a standard solution to the sample. The change in mV reading was recorded for each addition and used to calculate the concentration of Imb solutions in its pure form and pharmaceutical dosage form.

In FIA conditions, the determination of the studied drug in its dosage form was made by preparing a series of solutions of different concentrations from the capsules and another for standard drug solution. The peak heights corresponding to these solutions were measured at the optimum FIA parameters related to the electrode used. The heights were then compared to those obtained from injecting standard solutions of the equivalent concentrations prepared from the pure drug at the same flow rate, sample loop and other flow conditions and the percentage recovery can be calculated as the ratio of the peak height of sample to that of equivalent concentration of standard drug.

For the analysis of capsules, the contents of 10 hard gelatin Gleevec® capsules (100mg Imb/cap) were mixed and appropriate weights were taken as samples and dissolved in 3 drops of 1M HCl, completed up to 50 mL with distilled water. Different concentrations were then prepared by appropriate dilution.

3. RESULTS AND DISCUSSION

3.1. Optimization of the electrode response under batch conditions

There are many factors that affect the performance of the electrode towards its ion, the most important of which are composition of the membrane, amount of ion-exchanger, ratio of the plasticizer, soaking time, effect of pH and presence of interferents.

Polyvinyl chloride (PVC) membranes plasticized using dioctylphthalate, the most commonly used plasticizer for PVC membranes, with a ratio (PVC:DOP 1:1), were prepared using the tetraphenyl borate as counter ion representing the active material for the drug-selective electrode investigated. The ratio of the membrane components (ion-exchanger, PVC, plactisizer) was varied till optimum composition, that is required for best performance in terms of slope of the calibration curve, usable concentration range and reproducibility of results, is attained. Each preparation was repeated three times to ensure reproducibility.

The results show that all electrodes have very short response time (less than 10 sec) and the composition with 10.00% Imb-TPB electrode exhibited the best Nernstian behavior, with slope of 57.58 mV/concentration decade with a usable concentration range of $1.0x10^{-5}$-$1.0x10^{-3}$ M, with limit of detection (LOD) 0.58 mg/L and limit of quantification (LOQ) 5.89 mg/L. The membrane electrode needs a kind of preconditioning through soaking in the drug solution before use because of its plastic nature. This improves the elasticity of the membrane surface at which the exchange process takes place. This preconditioning process requires different soaking intervals depending on diffusion and equilibrium at the interface and according to the physical properties of the membrane [31].

The slope of the electrode started with 55.80 mV/concentration decade after 30 minutes. It reached 57.58 mV/concentration decade after 24 hrs, then decreased gradually reaching 53.42 mV/concentration decade after 48 hrs. The slope reached 52.63 mV/concentration decade after 6 days and continues decreasing to reach 50.73 mV/concentration decade after 10 days, dropping to 47.70 mV/concentration decade after 21 days and finally 44.17 mV/concentration decade after 30 days. It is recommended to soak Imb-TPB electrode in Imb solution for 1 hr before use in order to reach an optimum slope very close to the Nernestian value and it was found that when the electrode is kept dry in the refrigerator, the Nernestian slope was maintained for intervals reaching several months.

3.2. Optimization of the electrode response in FIA Conditions

FIA parameters (sample volume, flow rate, reactor length and size [32]**,** that affect the response of an ion-selective electrode on operation in FIA condition should be studied and taken into consideration on designing the flow system.

Samples of different volumes (70 to 230 µL) were injected into the flow stream, which highly affect the dispersion process. Sample volume of 70 µL was the optimum as it requires shorter time to recover the base line and lower consumption of reagents [33].

Studying the flow rate is essential as the peak heights and time required to recover the base line depend on it. The response of the investigated electrode to a solution with concentration $1.0x10^{-2}$ M Imb was measured at different flow rates (5.00-10.00 mL/min). As the flow rate increases, the residence time of the sample decreases requiring less time to recover the baseline, so the peaks are sharper and higher, but this will consume more carrier, which in this case is water. A flow rate 9.00 mL/min was used as the optimum rate, which allows faster recovery of the base line especially in high concentrations with shorter time of analysis and less consumption of the carrier. The composition of the carrier should be as similar as possible to that of sample to ensure base line stability, response time

and wash characteristics [34, 35]. Water was used as a carrier in a one-channel manifold FIA system in this work. The base line attainment for the studied electrode takes very short time.

Dispersion coefficient (D), is one of the most important factors that should be considered on constructing a FIA system because it shows how much the original sample solution is diluted on its way towards the sensor and how much time has elapsed between the sample injection and the readout. It is defined as the ratio of concentrate ions of sample material before and after the dispersion process has taken place. The dispersion coefficient was found to be 1.03, limited dispersion, (D = 1-3) which is preferable as the original composition of the sample is measured and the sample is diluted away from the detection limit of the ISE [36, 37].

An increase in the slope of the calibration plots in FIA was observed compared with batch measurements, as potential is measured under conditions very close to the equilibrium at membrane solution interface. The slope of the calibration graph reaches 65.70 mV/concentration decade under FIA conditions compared to 57.58 mV/ concentration decade in batch conditions for Imb-TPB electrode. The super-Nernstian sensitivities obtained in FIA measurements on using the investigated electrodes at different flow rates is due to the slow response of the electrode potential to concentration change especially when low concentrations are measured and depends on the state of the membrane surface at the interface with the measured solution. [37].

The usable concentration range in FIA for the electrodes was improved to cover the range $5.0x10^{-6}$-$1.0x10^{-2}$ M, compared to $1.0x10^{-5}$-$1.0x10^{-3}$ M in batch conditions. This can mainly be attributed to the difference in dispersion coefficients of the two techniques.

Fig. 2 represents the recordings (A) and its corresponding calibration curve (B) on using Imb-TPB electrode under optimum FIA conditions using degassed water as a carrier stream, sample volume of 70 µL, a flow rate of 9.00 mL/min, offering a dispersion coefficient of 1.03 (limited dispersion).

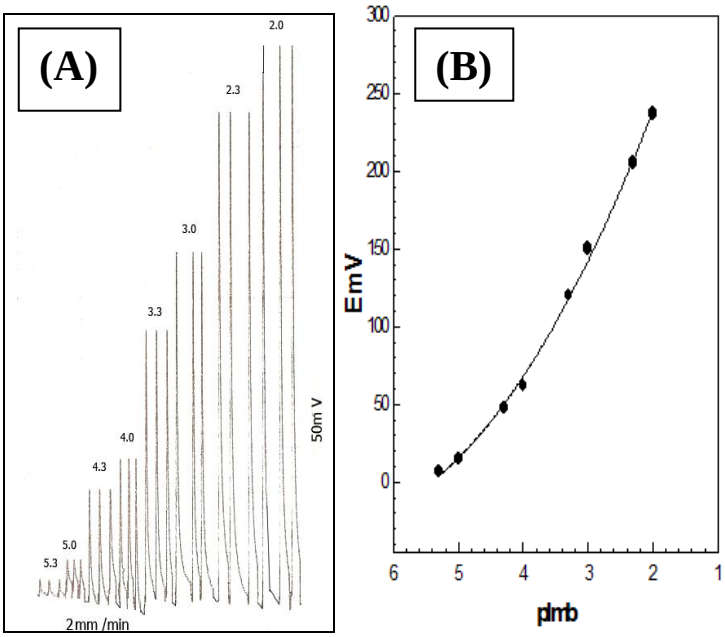

Figure 2. The recordings obtained for the flow rate 9.00 mL/min (A) and its corresponding calibration curve (B) on using Imb-TPB electrode.

3.3. Effect of pH on the response of the electrode

The effect of pH on the response of the electrode was studied under both batch and FIA conditions. The results indicate that pH change does not affect the potential readings in batch conditions within the range 4.00-7.50. While in FIA, the peak heights representing the pH are almost stable in the range 4.00-6.00, so the electrode can be used safely in these ranges. The potential decreases gradually above these ranges in both conditions due to the release of free base in the solution, leading to a decrease in the concentration of the detected imatinib cation. While at pH values lower than these ranges in both conditions, the potential increases gradually may be as a result of increase of protonated species and dependency of potential on the pH of the solution [31, 38**].**

3.4. Selectivity of the electrode

The term selectivity coefficient $K^{pot}_{Drug,J^{z+}}$ is the main source of information concerning interferences on the electrode response. It must be very small, so that the electrode exhibits a Nernstian dependence on the primary ion over a wide concentration range of the primary ion increasing the selectivity of the electrode towards this ion. The selectivity of the membrane electrode depends on ion selectivity of the ion exchange process at the membrane test solution interface.

The electrode response towards different substance and ionic species as inorganic cations and neutral compounds as urea and creatinine that can be present in biological samples was indicated in batch and FIA conditions and the values of selectivity coefficients, are given in Table 1.

In batch conditions, the separate solution method [SSM] [28], was used mainly to determine the selectivity coefficient value for inorganic cations. Although, it is still the simplest way to show whether interference takes place or not and is used to perform measurements in important biological samples [39]. This method cannot be used in case of uncharged species. A considerably high concentration of the interferent ion is used ($1.0x10^{-2}$ M) to ensure that there will be no interference if lower concentrations than this are present.

The matched potential method [MPM] [29], was also used to determine the selectivity coefficient for neutral interferents as sugars and also in FIA, where the sample remains in contact with the electrode for a short period of time, the selectivity coefficient is expected to be different from that found at batch conditions [40]. It is clear that the investigated electrode is highly selective towards the respective drug where the values ranged from 1.50-3.23 in batch and from 3.00-(>4.00) in FIA.

In FIA condition, some of the interfering ions were out of the detection limit of the electrode and the peaks of those interferants were shorter than the peak of $5.0x10^{-6}$ M solution of the drug as in case of $NaHCO_3$, Na_2SO_4, trisodium citrate, glucose and urea that is why their selectivity coefficient value is indicated by >4.00, after applying the matched potential method, which is the minimum concentration to be measured using the electrode.

Table 1. Selectivity coefficient of Imb-TPB electrode under batch and FIA conditions.

$-\text{Log}\, K^{pot}_{Drug,J^{z+}}$			
Interferant	**Batch**		**FIA**
	***SSM**	****MPM**	
BSA	---	**2.07**	**3.30**
Glucose	---	**2.50**	**>4.00**
Hepes	---	**1.57**	**3.00**
Urea	---	**2.70**	**>4.00**
NaH_2PO_4	**2.02**	---	**3.30**
Creatinine	---	**2.86**	**>4.00**
NH_4Cl	**2.61**	---	**3.30**
$MgSO_4$	**1.50**	---	**3.30**
Na-citrate	**2.90**	---	**>4.00**
$NaHCO_3$	**3.23**	---	**>4.00**
$CaCl_2$	**1.80**	---	**3.00**
$MgCl_2$	**1.70**	---	**3.30**
Na_2SO_4	**2.56**	---	**>4.00**
KCl	**2.50**	---	**3.30**
NaCl	**2.66**	---	**>4.00**

*SSM: Separate Solution Method
**MPM: Matched Solution Method

For neutral molecules as glucose, urea and creatinine, in both conditions, the high selectivity is mainly attributed to the difference in polarity and to the lipophilic nature of their molecules relative to imatinib ion [41, 42].

On comparing the results of batch and FIA conditions, it is found that the electrode exhibits better selectivity in FIA due to the short contact time of the interferant with the membrane surface, less chance of penetration and contamination of the membrane surface.

3.5. Analytical applications

In order to be able to use the proposed ion-selective electrode in quantitative analysis in batch and FIA conditions. The standard additions methods in batch measurement and peak heights comparison under FIA conditions were applied.

3.5.1. Standard Additions Methods in Batch conditions

The developed electrode has been used for the determination of imatinib mesylate in its pure form and its pharmaceutical preparation (Gleevec® 100mg/capsule) by applying standard additions method where small increments of $1.0x10^{-2}$ M standard Imb solution were added to 25 mL distilled water containing 0.14-14.70 mg imatinib mesylate with concentrations (1.0×10^{-5}-1.0×10^{-3} M). The results in Table 2, show that the recovery % values for pure form of the drug ranged from 99.00-102.70% with coefficient of variation ranging from 0.75-1.22 for Imb-TPB electrode. While for Gleevec®capsules (dosage form), the recovery value ranged from 99.35-101.60% with coefficient of variation ranging from 0.68-1.24.

The values are very close to the taken amounts as indicated in the drug pamphlets reflecting the high accuracy and precision of the electrode as sensor for the drug.

Table 2. Determination of imatinib in its pure form and pharmaceutical preparations using standard additions method under batch conditions.

Sample	Taken (mg)	Found (mg)	Recovery%	RSD%(Relative standard deviation three determinations)
Pure solutions				
	0.14	**0.14**	**99.30**	**1.20**
	0.73	**0.73**	**99.00**	**0.75**
	1.47	**1.47**	**100.27**	**0.93**
	7.37	**7.57**	**102.70**	**1.22**
	14.70	**15.00**	**102.00**	**0.97**
Gleevec® capsule (100mg/cap.)	**0.14**	**0.14**	**100.00**	**0.68**
	0.73	**0.74**	**101.60**	**1.07**
	1.47	**1.48**	**100.80**	**1.24**
	7.37	**7.32**	**99.35**	**0.99**
	14.70	**14.62**	**99.50**	**0.97**

3.5.2. Potentiometric Determination Using Peak Height Comparison under FIA conditions

Under FIA conditions, a series of solutions of different concentrations from the capsules (5.0×10^{-6} M-1.0×10^{-2} M) containing 0.07-147.42 mg imatinib that were measured at optimum flow rate (9.00 mL/min) using Imb-TPB electrode then compared to their corresponding from standard solutions

of the pure drug at the same flow rate and using the same sample loop and other flow conditions as given in Table 3.

The results show that the recovery % ranged from 98.30-102.40 % with coefficient of variation from 0.30-0.64. Peak heights for solutions prepared from (Gleevec® capsules) are very close to those of equivalent concentrations of the drug as given in the drugs pamphlets indicating high accuracy and precision of the determination.

3.5.3. Statistical Analysis and Validity of the Proposed Method

In order to be able to ensure that the proposed method is valid and applicable, the obtained value for the amount of the analyte should be very close to the actual value.

The accuracy indicates how close is the measured quantity to its actual (true) value, while precision, is the reproducibility or repeatability. The precision and accuracy of the method were investigated via inter and intraday repeatability of imatinib mesylate, three replicated at the limit of quantitation range. The precision and accuracy of the method are expressed as RSD and recovery %, also reproducibility (day to day) was investigated. Relative standard deviation less than 1.30 % for Imb-TPB electrode was obtained [43].

Table 3. Determination of imatinib in pharmaceutical preparations applying peak heights comparison under FIA conditions

Sample	Taken (mg)	Found (mg)	Recovery%	RSD%(Relative standard deviation three determinations
Gleevec® **Capsule (100mg/cap.)**				
	0.07	**0.07**	**100.00**	**0.50**
	0.14	**0.13**	**98.30**	**0.55**
	0.74	**0.74**	**100.00**	**0.57**
	1.47	**1.50**	**102.40**	**0.30**
	7.37	**7.37**	**100.00**	**0.64**
	14.74	**14.62**	**99.20**	**0.33**
	73.71	**73.41**	**99.60**	**0.42**
	147.42	**147.12**	**99.80**	**0.30**

Under batch conditions, the limit of detection (LOD) of the electrode was studied. It is defined as concentration corresponding to the intersection of the extrapolation of the linear part of the calibration curve with a value of 0.58 mg/L, while the limit of quantification (LOQ), defined as the last point corresponding to the intersection of the linear part of the calibration curve, was found to be 5.89 mg/L [31].While under FIA conditions, the LOD value was found to be 0.14 mg/L and LOQ values was found to be 2.95 mg/L.

The difference between the obtained and expected value is expressed in terms of recovery %. The student t-test and the F-test can be employed to decide whether the difference between the results obtained by the proposed method and a reference method [22] is accounted for by random errors and for the comparison of the standard deviation of the two methods [31, 44]. The one tail F-test method is used in comparison.

Comparing the obtained F-and t-values with the tabulated ones as shown in Table 4, the obtained values were lower than the theoretical tabulated values, so there was not any significant differences in the applied method in comparison to those of the referenced method [22], indicating the accuracy and precision of the present work. This reference method is based on the formation of the ion pair complex of imatinib with bromocresol green in acidic buffer followed by their extraction in chloroform and the absorbance was measured at 417 nm against the reagent blank. The following results were obtained as in Table 5 after carrying out the experiment.

Table 4. Statistical treatment of data obtained for the determination of Imatinib using Imb-TPB electrode, in comparison with the reference method.

	Imb-TPB		**Reference method [22]**
	Batch	**FIA**	
Pure solutions			
Mean ± S.D.	**100.6 ±1.01**	**---**	**99.87 ± 0.93**
F-test (4,3)	**1.22 (9.11)**	**---**	**---**
Student t test	**1.14 (1.53)**	**---**	**---**
Probability	**0.10**	**---**	**---**
Gleevec® (100mg/cap.)			
Mean ± S.D.	**100.25 ±0.99**	**99.91 ± 0.45**	**99.87 ± 0.93**
F-test (4,3)	**1.13 (9.11)**	**4.27 (4.34)**	**---**
Student t test	**0.59 (1.53)**	**0.08 (1.41)**	**---**
Probability	**0.10**	**0.10**	**---**

Table 5. Reference method for determination of imatinib mesylate.

Amount taken (µg/10mL)	Average Absorbance* at 417 nm (Average of 2 experiments)	Amount found (µg/10mL)	Recovery %
15.00	0.38	15.16	101.00
25.00	0.62	24.76	99.04
30.00	0.75	30.20	100.60
40.00	0.98	39.54	98.90
		Mean	99.87
		S.D	0.93
		S.E	0.46

The ruggedness of the potentiometric method was evaluated by carrying out the analysis using two different instruments on different days. The RSD of less than 1.30 % was observed for repetitive measurements in three different day time periods using two different instruments. The results indicate that the method is capable of producing results with high precision [45].

The robustness of the method was explained by the evaluation of the influence of small variation of variables including pH, potential range and measuring time. The results showed that the method is robust, results are stable in the pH range around 4.00-7.50 under batch conditions and 4.00-6.00 under FIA conditions.

A simple linear regression for the observed drug concentrations against expected values (5 points) was performed to show if the designed electrode exhibit any bias. The slopes of the regression lines are near to those of the ideal value of unity. While the intercepts were very small indicating that there is no systematic difference between determined and expected concentrations within the investigated range using the proposed method, Table 6 represents the results of the linear regression analysis for potentiometric determination of Imb under batch and FIA conditions using Imb-TPB electrode.

Table 6. Linear regression analysis for potentiometric determination of imatinib in batch and FIA conditions using Imb-TPB electrode

Imb-TPB	Intercept of regression line*	Slope of regression line	Correlation coefficient (r^2)
Pure solutions	-0.009	1.022	0.999
Gleevec® (100mg/cap.)	a) 0.009	0.993	0.999
	b) 0.003	1.000	0.999

*Observed versus theoretical.

a) Batch conditions. b) FIA conditions.

4. CONCLUSION

A new ion-selective electrode of plastic membrane type based on the formation of ion pair between the analysed drug and sodium tetraphenyl borate was developed. The life span of the electrode is 30 days on continuous soaking and several months when kept in dry conditions. It is characterized by usable concentration range of (1.0×10^{-5}-1.0×10^{-3} M) and (5.0×10^{-6}-1.0×10^{-2} M) in batch and FIA conditions, respectively. The change of pH does not affect the potential reading or peak heights of the electrode in the range of 4.00-7.50 in batch condition. While in FIA, the peak heights representing the pH are almost stable in the range 4.00-6.00. The electrode is highly selective towards many inorganic cations, and neutral molecules.

The presented electrode can be applied for the determination of its respective drug with nearly the same precision and accuracy in both batch and FIA conditions, but the use of FIA lead to shortening the time required for analysis. Thus the proposed method is simple and suitable for routine determination of the drug, it provides economic procedures, less time consuming and more sensitive compared with other reported spectrophotometric method (reference method).

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