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REVIEW ON ANALYTICAL TECHNIQUES USED FOR DETERMINATION OF ISOPROTERENOL HYDROCHLORIDE IN PHARMACEUTICAL DOSAGE FORMS AND BIOLOGICAL MATRICES

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ABSTRACT

The pharmaceutical analysis deals with qualification and quantification analysis of active pharmaceutical ingredients in pharmaceutical dosage forms and biological matrices. A good literature survey helps to focus on earlier published research and review papers in order to complete the good review work. Isoproterenol hydrochloride is a non-selective β-adrenoreceptor agonist used as medication in the treatment of bradycardia and asthma. Several reviews and research papers published from various journals have been collected and combined for our review work. In this review, we discuss some analytical techniques such as spectrophotometry, spectrofluorimetry, electrochemical method, high-performance liquid chromatography (HPLC), LC-MS/MS and gas chromatography for quantification of isoproterenol hydrochloride. When compared to other analytical techniques, it was found that the HPLC technique is most preferably used for analysis.

KEYWORDS

Isoproterenol hydrochloride, Isoprenaline, Bradycardia, Asthma and HPLC.

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INTRODUCTION

Optically active arylethanolamines are an important class of bioactive compounds widely used as class-II β-blocker, class-III antiarrhythmic, adrenergic, anthelmintic and antidepressant agents[1,2]. The drug was approved by the Food and Drug Administration (FDA) as a non-selective β-adrenergic agonist and Trace-amine associated receptor 1 (TAAR1) agonist under the trade name, Medihaler-Iso and isuprel, in January, 1982. It is used mostly to treat bradycardia, heart block, chronic obstructive pulmonary diseases

and rare in asthma and as an active bronchodilator[3,4]. Several methods have been reported to identify isoproterenol hydrochloride and its metabolites in biological samples such as high-performance liquid chromatography (HPLC), liquid chromatography-mass spectrometry (LC-MS)[5,6], gas-liquid chromatography (GLC)[7] and chemiluminescence determination using luminol-diperiodatoargentate (III)[8]. A sensitive spectrophotometric method recently has been developed for the determination of isopropyl amine, a core moiety of isoproterenol hydrochloride, at the trace level in pharmaceutical drug substances[9]. Bradycardia is a condition in which the individual has a resting heart rate of fewer than 60 beats per minute in adults. The symptoms of bradycardia include tiredness, confusion, dizziness, fainting and also includes pain in the chest and difficulty in breathing. Bradycardia will not show any of these symptoms until the heart rate drops below 50 beats per minute. Bradycardia is a problem in which the heart does not pump enough oxygen-rich blood to the circulatory system. The main causes for bradycardia include, a problem in the sinoatrial node in the heart which is known as the pacemaker, heart attack, tissue damage in the heart, hereditary heart diseases and also occurred by a problem in the conduction of electrical impulses from the aorta to the ventricles in the heart and abnormal metabolism of thyroid glands (hypothyroidism). Sleep disorders and rheumatic fever may also cause bradycardia. The treatment of bradycardia in mild conditions includes giving medications in which the individual does not need pacemaker until, in serious situations, isoproterenol hydrochloride injection is given in intramuscular or intravenous route. The preventive measures include, avoiding smoking, doing regular exercise and water intake can prevent you from bradycardia[10].

Isoproterenol Hydrochloride

Isoproterenol Hydrochloride is the hydrochloride salt form of isoproterenol, a synthetic catechol compound and potent beta-adrenergic agonist with a peripheral vasodilator, a bronchodilator and cardiac stimulating properties. Isoproterenol exerts its effect on the beta-1 adrenergic receptors in the myocardium, thereby increasing heart rate and cardiac output. In addition, isoproterenol acts on beta-2 adrenergic receptors in bronchiolar and vascular smooth muscle, thereby causing smooth muscle relaxation. Isoproterenol hydrochloride is an odorless white crystalline powder. Slightly bitter taste. Aqueous solutions turn brownish-pink upon prolonged exposure to air. Isoproterenol hydrochloride is a non-selective beta-adrenergic receptor agonist that has a molecular weight of approximately 247.72g/mol. The IUPAC name of isoproterenol hydrochloride is 4-[1-hydroxy-2-(propan-2-ylamino) ethyl] benzene-1, 2-diol; hydrochloride (Figure No.1) having molecular formula C11H18CINO3 and melting point at 338 to 340 0F[11].

MECHANISM OF ACTION

Isoproterenol hydrochloride is a potent non-selective beta adreno-receptor agonist that stimulates both β1 and β2 receptors. This drug reduces peripheral vascular resistance in the skeletal muscles and when given intravenously it lowers the broncho-spasms which occur due to anesthesia. The β agonist bind to receptors in the smooth muscles and then produces relaxation of these muscles and in the liver they promote glycogenolysis and in the kidneys, they tend to release renins. In vascular smooth muscles, it increases the cyclic adenosine monophosphate (cAMP) results in smooth muscle relaxation this is because that cAMP blocks a myosin light chain kinase reaction which is responsible for phosphorylation of smooth muscle myosin. The drug molecule binds with β adreno-receptors in the heart muscles and coupled to the GS proteins which activate the adenylyl kinase enzyme and produce cAMP from ATP. This cyclic-AMP activates protein kinase which is responsible for phosphorylating the calcium channels, which will result in the entry of calcium ions in the cells thus activating the sarcoplasmic reticulum to produce contraction of the heart muscles[10].

ANALYTICAL TECHNIQUES FOR DETERMINATION OF ISOPROTERENOL HYDROCHLORIDE

Some of the analytical techniques include ultraviolet spectroscopy, fluorimetry, mass spectroscopy, high-performance liquid chromatography, gas chromatography, etc. The analytical method development is the most important process in which the suitable analytical method is selected for analysis of drug in dosage forms and biological samples which produce the desired results. The analytical method development includes the selection of mobile phase, stationary phases and suitable columns in cases of HPLC method of analysis. The method validation is important in which the suitable analytical method is validated according to the guidelines in the pharmaceutical industry. The validation parameters include selectivity, linearity, accuracy, precision, sensitivity, the limit of quantification, the limit of detection and so on. In other cases, these highly modern analytical equipment have been coupled to produce more desired results which can elaborate more detailed information of the pharmaceutical drug.

Spectrophotometry

Solich P *et al*. Developed a new spectrophotometric method with automated flow injection for the determination of epinephrine and isoproterenol in pharmaceutical preparations. The isoproterenol reacted with Fe (II) in the presence of amino acid carbonate buffer (pH 8.3) and formed a colored complex. The maximum absorbance of the colored product was measured at 530nm. The calibration graph was constructed that shows a linear range from 10 to 300mg/L for isoproterenol. The method was validated and found to be sensitive, accurate, precise, and reproducible. The limit of quantification (LOQ) of the drug was 4mg/L. This method was useful to determine the assay and content uniformity of drug in tablet dosage forms[12].

Shabouri El Salwa R *et al*. proposed a spectrophotometric method for quantification of isoprenaline sulfate in a tablet dosage form. In this method, the isoprenaline sulfate was oxidized with silver oxide in an aqueous solution to form amino chrome (a red color compound). The maximum absorbance of the red color product (stable for 2 hours) was found to be 490nm. The method was validated and found to be specific and selective with good recovery. The linearity of the drug concentration ranges from 5 to 80ng/mL. This method was also suitable for studying stability (oxidative degradation) studies[13].

Kaistha KK developed the di (2-Ethylhexyl) phthalate (DEHP) method and sodium meta periodate method for the determination of isoproterenol and isoproterenol sulfonic acid from decomposed inhalations and injections by using a suitable analytical method. The preparations of both standard and sample solutions were carried out for analysis. The principle of the DEHP method involves the formation of an ion pairs. The unchanged form of the drug was reacted with DEHP in presence of potassium phosphate buffer (pH 5.8). The isoproterenol was determined from the organic phase and sulfonic acid of isoproterenol was determined from the aqueous phase. The isoproterenol sulfonic acid was quantified by using Doty's reagents. The sodium meta periodate method was used to quantify isoproterenol by reacting aryl aldehyde with an unchanged drug. Both methods were detected by UV spectroscopy. The method was validated and found to be specific and precise[14].

Spectrofluorimetry

Shan-Bao Qiao developed a spectrometric method based on fluorescence detection. The drug isoprenaline was treated with a buffer solution of pH (6.80) and analyzed. The wavelength at which the drug excites was found to be 287nm and the emission wavelength was found to be 622nm. The method was validated and the linearity of drug concentration ranges from 0.1 to 2.3mg/L. The detection limit of the drug by this method was found to be 0.0087mg/L. This method was simple, accurate and successfully applied for analysis[15].

Prasad VK *et al*, proposed the spectrofluorometric method for the determination of isoproterenol hydrochloride in injection form. In this method, isoproterenol HCL was reacted with iodine potassium iodide buffer at pH 4.0 and oxidized. The

partially oxidized form of the drug was converted into a fluorescent (Lutin) compound by reacting with strong alkali and was subjected for analysis. The effect of various reagents used in this method was studied. Thus, the simple, specific method was developed for successful analysis to determine isoproterenol and its degradation compounds[16].

Guanbing *et al*. proposed a simple flow injection chemiluminescence (CL) method to detect isoprenaline hydrochloride and some β2 adrenergic drugs in pharmaceutical preparations. The isoprenaline hydrochloride was reacted with potassium ferricyanide- luminol and detected by CL. The 1mmol/L of potassium ferricyanide was introduced into the pipeline and the mixture of 10µmol/L of luminal and 1.2mmol/L of sodium hydroxide was injected into the flow system. The flow speed was set at 2.6mL/min and the intensity of emission CL was detected by a photomultiplier tube. The method was validated and found to be linear, robust and the limit of detection (LOD) for isoproterenol was 5ng/mL[17].

Electrochemical Method

Ali A Ensafi *et al*, proposed an analytical method for the identification of isoproterenol in the presence of uric acid using p-chloranil carbon nanotubes paste electrode. The concentration of isoproterenol and uric acid can be determined based on electrochemical potential difference. Here, isoproterenol was oxidized by p-chloranil at a pH 10.5 and the potential difference for estimation of isoproterenol and uric acid was set at 360mv and was analyzed. The linearity ranges from 0.015 to 100µmol/L for isoproterenol and 3.0 to 310µmol/L for uric acid. The detection limit was found to be 0.009µmol/L for isoproterenol and 2.3µmol/L for uric acid. This method was useful for the estimation of isoproterenol and uric acid from urine samples and injection ampoules[18].

Mazloum ardakani *et al*, proposed an electrochemical method for the determination of isoproterenol along with acetaminophen and folic acid in the combined form. Here a new carbon pasted electrode containing (E)-2-((2-chlorophenylimino methyl) benzene-1, 4-diol (CD) and titanium dioxide nanoparticles were used as a sensor for the identification of isoproterenol. The isoproterenol was detected by the change in electrical potential difference by oxidation of isoproterenol at 235mv. The detection limit of the drug was found to be 3.7µM. The isoproterenol was quantified by the standard addition method and was useful for analysis[19].

High Performance Liquid Chromatography

Neeraj Kumar *et al*, developed two methods, reversed-phase (RP) ultra-high-performance liquid chromatography (UHPLC) and liquid chromatography coupled with a mass spectrometer (LC-MS) for determination of isoproterenol and related substance (4-[2- (propan-2-ylamino) ethyl] benzene-1, 2-diol (Imp-II) in isoproterenol hydrochloride. For the UHPLC method, the chromatographic separation was carried out in Agilent Zorbax Rx C8 column (250 × 4.6mm, 5µm) using 0.1% trifluoroacetic acid with triethylamine (pH 3.0) and acetonitrile (gradient elution) as mobile phase at 1mL/min flow rate. The impurity was detected by a diode array detector (DAD) at 280nm. The structure of the impurity-II was determined by the LC-MS method. Before analysis, the selected impurity was isolated by using a semi-preparative HPLC method. The chromatographic separation was carried out in Inert Sustain Swift C18 column (250 × 20mm, 5µm) using 0.1% aqueous acetic acid: acetonitrile (95:5, v/v) as mobile phase and photodiode array (PDA) detection at 280nm was used to monitor the compounds in a column. Thus, the impurity was isolated and the structure was determined by LC-MS method using Thermo Accucore MS C-18 column (150 × 4.6 mm, 2.6µm) with 0.1% aqueous trifluoroacetic acid: methanol (gradient elution) as mobile phase. The electrospray ionization method was used as an ion source and the drug was analyzed by ion trap MS analyzer. The retention times of isoproterenol and impurity-II were found to be 5.61 and 5.80 mins respectively. The mass to charge ratio (m/z) was found to be 212.14 (for isoproterenol) and 196.10 (for Imp-II). Thus the structure of impurity was determined and it was confirmed by using nuclear magnetic resonance (NMR) and Fourier transform-infrared (FT-IR) spectroscopy. For NMR,

deuterated methanol was used as a solvent and tetramethylsilane (TMS) was used as the internal standard. For IR, the pellet pressing method with potassium bromide was used for sample preparation and IR spectra were scanned from 4000 to 40cm-1[20].

Li-jul Yu *et al*, analyzed the distribution of droplet size and isoproterenol hydrochloride in the aerosol by the HPLC method. The chromatographic separation was carried out in shim pack VP ODS column (250 × 4.6mm×5µm) using mobile phase (1.76g of sodium 1-heptane sulfonate dissolved in 800mL of water and 200mL methanol and pH 3.0 was adjusted by adding 1mol/L phosphoric acid) and detected by UV detection at 280nm. The method was validated and found to be selective, sensitive and accurate with good recovery. The linearity of the drug ranged from 3.5 to 700µg/mL[21].

Xiang mingfeng *et al*, described an analytical method that is helpful in determining the isoprenaline hydrochloride injection content and also to analyze the radiation affecting the content of the injection. In this study, the HPLC method had been developed and the separation was carried out in a column using mobile phased containing 0.22% of heptane sulfonic acid sodium solution with phosphoric acid (pH 3.0): methanol (55:45) and the flow rate was adjusted to 1mL/min. The detection wavelength was set at 280nm. The method was validated and the linearity of this drug ranged from 2.5 to 12.5µg/mL. The recovery was found to be 95%-105% and the precision was less than 2. While conducting these experiments, it was found that the content of the isoprenaline hydrochloride in injection was decreased due to irradiation, thus the method is suitable for the identification of isoproterenol content in injection[22].

Smith G *et al*, proposed an HPLC method for the determination of isoproterenol in injection form. The influence of ascorbic acid and ethylenediaminetetraacetic acid (EDTA) affecting the stability of the drug was also studied. The separation was carried out in ODS hypersil -5 column (100 ×4.5mm) using methanol: acetic acid: sodium lauryl sulfate: water (30:2:0.002:68) as mobile phase at 1.4mL/min flow rate and was detected by UV detection at 280nm. The linearity of the drug concentration ranges from 0.18 to 0.8mg/mL. This method was most suitable for analysis not affected by any degradation products[23].

Lee Elrod *et al*, proposed an HPLC method for quantification of isoproterenol in pharmaceutical formulations. The chromatographic separation was carried out in nucleoside C18 column (15cm ×4.6mm) using 0.05M phosphate buffer with 5mM pentane sulfonic acid, sodium, and 0.1mM disodium EDTA (pH 3.6): methanol (90:10) as mobile phase at 1mL/min flow rate. The drug was detected by the electrochemical detector. The method was validated. The linear response of the drug was found at 42.9ng/mL and its recovery was 82 to 98%[24].

Hjemdahl P *et al*, developed a sensitive HPLC method for quantification of isoproterenol in human plasma samples. The analyte was extracted and separated in a strong cation exchange column (25cm × 4mm) using a mobile phase containing 0.1M acetate-citrate buffer (pH 5.2) with 1.5 to 2mL/min flow rate and detected by electrochemical detection. The detection limit of the analyte was found between 0.05-0.1nM and contain recovery at 60-70%[25].

Vashistha Vinod Kumar *et al*, developed an RP-high performance liquid chromatography (HPLC) method for quantification of enantiomers of isoprenaline in human plasma samples. The analyte was extracted and derivatized with chiral s-triazine to form diastereoisomers and was subjected for analysis. The separation was carried out in Li Chrospher C18 column (25cm × 4.6mm, 5µm) using acetonitrile and 0.1% aqueous trifluoroacetic acid (gradient elution) as mobile phase and flow rate at 1mL/min. The enantiomers were detected at 254nm by an ultraviolet (UV) detector. The method was validated and LOD was found to be 24.6ng/mL and 26.8ng/mL for 2 enantiomers of isoprenaline[26].

Liu –Yi-Wei *et al*, developed an HPLC method for the determination of isoproterenol concentration in the mouse plasma using dihydroxy benzyl-amine as internal standard (IS). The separation of analyte was carried out in Symmetry Shield C18 column (250 ×

4.6mm×5µm) using 0.05mol/L citric acid monohydrate: 0.05mol/L anhydrous sodium acetate: 0.3mmol/L disodium ethylene diamine tetraacetic acid: 1mmol/L IPR-B8: 0.06mmol/L dibutyl amine and 1.6% methanol as mobile phase at 0.9mL/min flow rate and detected by electrochemical (EC) detector. The method was validated and found to be sensitive, linear, precise and accurate. The LOD of the analyte was 0.08ng/mL and this method was useful for pharmacokinetic studies[27].

LC-MS/MS

Liquid chromatography (LC) is coupled with tandem mass spectroscopy (MS/MS) for better detection with good resolution. Jiawei Zhou *et al.* developed an LC-MS/MS method for quantification of isoproterenol in rat plasma using diazepam as IS. The analyte was extracted and separation was carried out in Shim-pack XR-C8 column (100 × 2mm, 2.2µm) using acetonitrile and 0.05% formic acid (gradient elution) as mobile phase at 0.3mL/min flow rate and analyzed by triple quadrupole analyzer. The electrospray ionization (ESI) method was used as an ion source. The analyte and IS was detected by multiple reaction monitoring (MRM) mode. The m/z of analyte and IS was 212.1 to 193.9 (for analyte) and 285.2 to 193.2 (for IS). The method was validated and found to be selective, linear, accurate and precise[28].

Gas chromatography (GC)

Watson *et al*, developed a gas-liquid chromatography (GLC) method to determine isoproterenol and two drugs in pharmaceutical formulations. The drug was derivatized with trimethylsilylating reagent for analysis. The separation was carried out in a U-shaped methyl silicone glass column (1.82m × 6mm, o.d) using nitrogen as a carrier gas and the flow of gas was adjusted to 70mL/min. The injector, column, and detector temperature was set at 225, 170 and 225ºC. The drug was detected by flame ionization detector (FID) and the recovery value was found to be 94.9-103.4%. The structures of the three drugs were confirmed by IR and NMR spectroscopy[7].

Tian Miao analyzed beta-agonists from the pork animal tissues by gas chromatography combined with mass spectroscopy. In that, isoproterenol was one drug. The sample was extracted from the tissue by liquid-liquid extraction (LLE) method using sodium acetate buffer and separated at strata X -C cation exchange column and was detected by MS. The method was validated. The correlation coefficient was found to be greater than 0.996, detection limits range from 1µg/kg to 5µ/kg for all the beta-agonists, the recovery of these compounds was found to be (59%-77%), RSD (0.87-7.0%), This method was found to be suitable for analyzing β agonists present in pig liver and kidney samples[29].

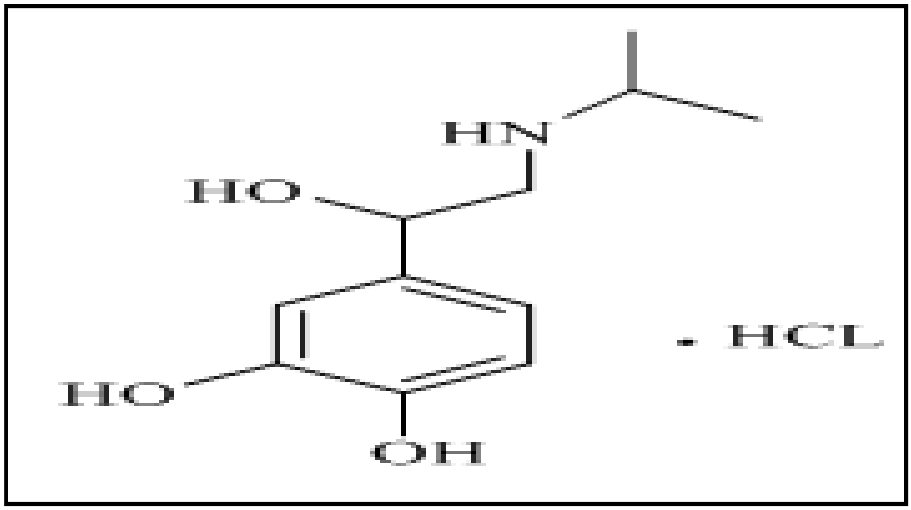

Figure No.1: Structure of Isoproterenol Hydrochloride

CONCLUSION

In this review, we described the various analytical methods such as spectrophotometry, spectrofluorimetry, electrochemical method and chromatographic techniques for quantification of isoproterenol in pharmaceutical dosage form and biological samples. Compare to all the above-mentioned techniques it was found that the HPLC technique was the most efficient and useful in analyzing isoproterenol. This study will be useful in gaining information for the researchers and students in future predictions in the research paper and review works.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBLIOGRAPHY

1. Szasz G, Budvari-Barany Z. Pharmaceutical chemistry of antihypertensive agents, *CRC Press, Boston,* 1, 1991, 1-275.
2. Brooks W W, Conrad C H. Isoproterenol-induced myocardial injury and diastolic dysfunction in mice: Structural and functional correlates, *Comp. Med,* 59(4), 2009, 339- 343.
3. Vilskersts R, Liepinsh E, Kuka J *et al.* Myocardial infarct size-limiting and anti-arrhythmic effects of mildronateorotate in the rat heart, *Cardi Dr The,* 23(4), 2009, 281-288.
4. Elesber A, Nishimura R A, Rihal C S *et al.* Utility of isoproterenol to provoke outflow tract gradients in patients with hypertrophic cardiomyopathy, *Am. J. Cardiol,* 101(4), 2008, 516-520.
5. Saprygina T V, Tsoi A N, V.G. Kukes. Determination of isoprenaline in blood plasma by HPLC with electrochemical detection, *Pharm. Che J,* 24, 1990, 681-683.
6. Quan-sheng, Min C H, Wei H *et al*. Research of the related substances in isoprenaline hydrochloride and its injection, *Chin. J. Pharm. Anal,* 32(5), 2012, 838-842.
7. Watson J R, Lawrence R C. Selective GLC determination of epinephrine, isoproterenol and phenylephrine in pharmaceutical dosage forms, *J. Pharm. Sci,* 66(4), 1977, 560-564.
8. Rezaei B, Ensafi A A, Haghighatnia F. A sensitive chemiluminescence determination of isoproterenol in pharmaceutical and human serum using luminodiperiodatoargentate (III), *Anal. Methods,* 4(6), 2012, 1573-1578.
9. Nagaraju C, Raja G, Kumar Ray U *et al*. A simple and sensitive spectrophotometric method for the determination of trace level mono isopropyl amine in pharmaceutical drug substances, *Int. J. Pharm. Sci. Res,* 7(2), 2016, 834-839.
10. Padmaja Udaykumar. Medical pharmacology, *CBS Publishers and Distributors,* 5th Edition, 2017, 144-180.
11. Isoproterenol hydrochloride [Internet], Pubchem.ncbi.nlm.nih.gov, 2020. https://dtp.cancer.gov/dtpstandard/servlet/dwindex?searchtype=NSC&outputformat=html&searchlist=757079.
12. Solich P, Polydorou C K, Koupparis M A *et al*. Automated flow-injection spectrophotometric determination of catecholamines (epinephrine and isoproterenol) in pharmaceutical formulations based on ferrous complex formation, *Journal of Pharmaceutical and Biomedical Analysis,* 22(5), 2000, 781-789.
13. Shabouri E l, Hussein S A, Abel Alim A M. Simple and rapid spectrophotometry method for determination of adrenaline and isoprenaline, *Journal of AOAC International,* 71(4), 1988, 764-767.
14. Kaistha K K. Selective determination of isoproterenol and isoproterenol sulfonic acid in pharmaceutical dosage forms, *Journal of Pharmaceutical Sciences,* 59(2), 1970, 241-248.
15. Shan-Bao Qiao. Direct determination of isoprenaline by fluorescence spectrophotometry, *Department of chemistry, Yancheng Teachers,* 2016.

16. Prasad V K, Ricci R A, Nunning B C *et al*. Improved, rapid spectrophotofluorometric method for assay of isoproterenol hydrochloride injections: A comparative study, *Journal of Pharmaceutical Sciences,* 62(7), 1973, 1135-1140.
17. Guangbin Zhang, Yuhai Tang, Jian Shang *et al*. Flow-injection chemiluminescence method to detect a β2 adrenergic agonist, *Luminescence,* 30(1), 2015,102-109.
18. Ensafi A A, Allafchian A, Reaei B. PVC membrane selective electrode for determination of isoproterenol based on naphthylethylenediamine dihydrochloride-tetraphenylboranuide, *Anal, Bioanal. Electrochem,* 7(5), 2015, 13-20.
19. Mazloum-Ardakani, Mohammad *et al*. Simultaneous determination of isoproterenol, Acetaminophen and folic acid using a novel nanostructure-based electrochemical sensor, *Electro Analysis,* 26(2), 2014, 275-284.
20. Neeraj Kumar, Subba Rao Devineni, Prasad Reddy Gajjala *et al.* Synthesis isolation, identification and characterization of new process-related impurity in isoproterenol hydrochloride by HPLC, LC/ESI-MS and NMR, *Jou of Pha Ana,* 7(6), 2017, 394-400.
21. Li-jul Yu, Hai-weil, Liu min *et al*. HPLC determination of droplet size distribution, Content of active ingredient in content of an actuation isoprenaline hydrochloride aerosol, *Chinese Journal of Pharmaceutical Analysis,* 28(6), 2008, 945-948.
22. Xiang Mingfeng, Lu Hua, Guan Haiyan1and Xie Hong *et al*. Study on isoprenaline hydrochloride injection content change influenced by irradiance, *Department of Pharmacy, Field Surgery Research Institute of Daping Hospital, Third Military University*.
23. Smith G, Hasson K, Clements J A. Effects of Ascorbic acid and disodium edetate on the stability of isoprenaline hydrochloride injection, *Journal of Clinical Pharmacy and Therapeutics,* 9(3), 1984, 209-215.
24. Lee Elrod, Joseph Schmit L and James Morley A. Determination of isoproterenol sulfate on surfaces using high-performance liquid chromatography with electrochemical detection, *Journal of Chromatography,* 723(2), 1996, 235-241.
25. Hjemdahl P, Martinsson A and Larsson K. Improvement of the isoprenaline infusion test by plasma concentration measurements, *Life Sciences,* 39(7), 1986, 629-635.
26. Vashistha Vinod Kumar and Bhushan Ravi. Sensitive enantioseparation and determination of isoprenaline in human plasma and pharmaceutical formulations, *Biomed Chromatogr,* 33(8), 2019, 1-15.
27. LiuYi-wei, Wang Chang-lian and Huang Pin-fang. HPLC-ECD determination of isoproterenol concentration in mouse plasma, *Chinese Journal of Pharmaceutical Analysis,* 31(6), 2011, 1098-1101.
28. Jiawei Zhon, Hui Yin *et al*. Efficient and selective analytical method for the quantification of a β-adrenoceptor agonist, isoproterenol, by LC–MS/MS and its application to pharmacokinetics studies, *Journal of Liquid Chromatography and Related Techno,* 40(13), 2017, 699-705.
29. Liaoning and Tian Miao. Determination of β-Agonists Residue in Pork Tissues by Gas Chromatography. Available from: http:// en.cnki.com.cn/Article_en/CJFDTOTAL-TEST201007015.htmL.

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