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RESEARCH ARTICLE **OPEN ACCESS**

COMPREHENSIVE REVIEW OF ANALYTICAL AND BIOANALYTICAL STRATEGIES FOR THE DETERMINATION OF METOPROLOL SUCCINATE

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ABSTRACT

It belongs to a class of beta-blockers that is used to treat hypertension (high blood pressure) and angina (chest discomfort). The current research focusses mainly on the development of analytical and bioanalytical procedures, as well as the various techniques developed for the estimate of etoricoxib, whether in bulk or pharmaceutical dose form. Because they enable us to use sophisticated analytical techniques to acquire both qualitative and quantitative results, analytical methods are essential for determining compositions. Metoprolol succinate can be analyzed using spectroscopic, electrochemical, chromatographic, or hyphenated methods. These techniques minimize the effects of crucial process parameters on accuracy and precision while also assisting in their comprehension. The development of analytical methods is necessary to meet regulatory requirements and maintain high standards for the quality of commercial products. Standards and processes for granting approval, authentication, and registration have been established by regulatory bodies in a number of countries in response to the reference. The purpose of bioanalytical techniques is to measure the amount of a medication, metabolite, or common biomarker in a variety of biological fluids, such as tissue extracts, serum, urine, and saliva.

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INTRODUCTION

First licensed in 1992, this small molecule medication has six approved and seven investigational indications, with a maximum clinical trial phase of IV (across all indications). It is a selective beta-blocker used to treat heart disease patients' angina symptoms or reduce blood pressure. The market offers both immediate release tablets, prolonged release tablets, capsules dosage forms, and it is often administered orally. It is also available in injection forms for the immediate action to the patients. The oral formulations are available under the brand names as Metorol XL, Metocrest XL, Metaprole XR, Toprol XL, etc. It is generally available in 25 mg, 50 mg, 75 mg, 100 mg etc.(1)

Physicochemical properties: Metoprolol succinate is chemically, 1-[4-(2-methoxyethyl)-phenoxy]-3-(propan-2ylamino) propan-2-ol butanedioate (2:1).(2) It is a white crystalline powder, which is freely soluble in water, being a salt form of metoprolol.(3) It is soluble in methanol and sparingly soluble in ethanol. It is practically insoluble in acetone, diethyl ether and heptane. Its pKa is 9.7 and has a molecular weight of 652.8 g/mol.(4)

Pharmacokinetic: After delivery, peak plasma concentrations typically happen two hours later, followed by trough values six to twelve hours later. Just around 12% of the medication is bound to human serum albumin. Metoprolol has a half-life of three to seven hours. CYP2D6 is primarily responsible for the metabolism of metoprolol. The liver's biotransformation is the primary method of elimination. (5).

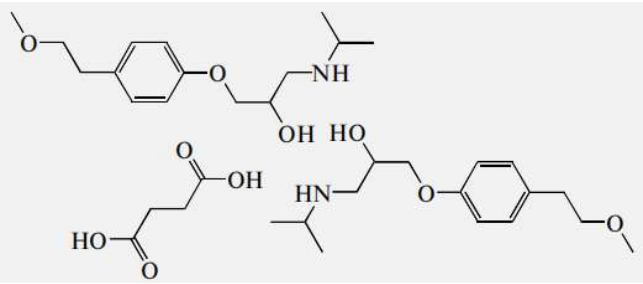

Figure 1. Chemical structure of metoprolol succinate

Pharmacodynamic: It is commonly known that metoprolol administration results in a dose-dependent decrease in cardiac output and heart rate in healthy persons. Reduced cardiac output, myocardial oxygen demand, and cardiac excitability all contribute to this outcome. Metoprolol suppresses the rate of atrioventricular conduction and lowers the slope of the pacemaker potential in the case of arrhythmias (6).

Table 1. Analytical method development using UV spectrophotometer

S. No.	Sample / Dosage form	Method / Instrument model	Solvent / Solution	Wavelength (nm)	References
1.	Tablet	Double beam UV/Visible spectrophotometer (1700), Shimadzu	Methanol: Water (80:20)	Method 1- 223 Method 2 – 257 Method 3 - 241	(10)
2.	Tablet	Double beam UV-visible spectrophotometer (Shimadzu-1800	Methanol	274	(11)
3.	Tablet	Double beam Agilent Cary UV spectrophotometer	Methanol:water (50:50v/v)	209	(12)
4.	Tablet	Shimadzu model 1700 (Japan) double beam UV/Visible spectrophotometer	Methanol	223	(13)
5.	Tablet	Shimadzu UV-1700 double beam spectrophotometer	Methanol	Method 1- 230.2 Method 2 – 231.8 Method 3 – 223 Method 4 - 282.4 & 284.6	(14)
6.	Tablet and bulk	UV double beam spectrophotometer of Shimadzu-1800	Methanol	223.40	(15)
7.	Tablet and bulk	Jasco UV-1800 UV spectrophotometer	Methanol	Method 1- 297 & 267.22 Method 2 – 275	(16)
8.	Tablet and bulk	UV-Visible Spectrophotometer (Jasco-V630)	Distilled water and phosphate buffer pH 6.8	221 and 223	(17)
9.	Tablet	Double beam UV/Visible spectrophotometer (Shimadzu model 2450, Japan)	Methanol	275.40	(18)
10.	Tablet	Shimadzu 1900i UV-visible double beam spectrophotometer	Methanol: 1N NaOH (1:1	224	(19)
11.	Tablet	Ultraviolet Double beam Spectrophotometer-systronics 2202	Methanol	224	(20)
12.	Tablet	UV double beam spectrophotometer of Shimadzu-1800	Methanol	223	(21)
13.	Tablet	Jasco double beam UV-spectrophotometer (Model: V-630)	Methanol	225	(22)
14.	Tablet	Shimadzu double beam UV-visible spectrophotometer (model 1800)	Methanol	Method 1 – 223 Method 2 - 230	(23)
15.	Tablet	Shimadzu UV/vis 1800 double beam spectrophotometer	0.1 N HCl	242	(24)
16.	Tablet and bulk	Shimadzu 1601 Double beam UV-Visspectrophotometer	Methanol	221	(25)

Table 2. Analytical method development using HPLC method

S.No.	Sample	Stationary phase/column	Mobile phase	Wavelength (nm)	Flow rate (ml/min)	RT (min)	Reference
1.	Tablet and bulk	C18 column (250 mm x 4.6 mm, 5 µm)	Acetonitrile: Phosphate Buffer pH 3.5 (40:60%v/v)	275	1.0	2.308	(27)
2.	Tablet	C18 Column (4.6 mm x 250mm, 5µm)	10 mM Phosphate buffer (pH 3): acetonitrile (50:50, v/v)	235	1.0	2.827	(28)
3.	Tablet and bulk	C18 (5 µm, 150 mm × 4.6 mm)	Acetonitrile and potassium dihydrogen phosphate buffer, pH 2.75 (70:30 v/v)	225	0.6	2.233	(29)
4.	Tablet	Cyano (250 mm × 4.6 mm, 5 µm)	Buffer (aqueous triethylamine pH 3) and acetonitrile (85:15 v/v)	254	1.0	4.6	(30)
5.	Tablet	C18G (250 x 4.6 mm, 5 µm) column	Methanol: Water in the ratio 80: 20, (v/v)	231	1.0	2.913	(31)
6.	Tablet and bulk	C18 5 µm column (250 x 4.6 mm)	Methanol: water (70:30 v/v)	230	1.0	3.8	(32)
7.	Tablet and bulk	C18 column 250X4.6 mm, 5 µm	Phosphate buffer (20 mM); acetonitrile (75:25)	215	1.0	5.672	(33)
8.	Tablet and bulk	C18 250 x 4.6mm, 5 µm	15mM ammonium acetate (pH 6.5): acetonitrile (58:42)	230	1.0	3.9	(34)
9.	Tablet	C-18 columns (250mm ×4.6mm, particle size of 5µm)	Methanol: Water: Acetonitrile (70:20:10)	222	1.0	2.1	(35)
10.	Tablet	ODS 3 column (100 × 4.6 mm, 5 µm)	Diammonium hydrogen phosphate buffer solution (at pH 5.5): Methanol (70:30 v/v)	254	1.0	6.91	(36)
11.	Tablet	C18 Column (250 X 4.6mm, 5µm particle size)	Acetonitrile and potassium di-hydrogen orthophosphate buffer (pH- 2.8) in the ratio 60:40v/v	220	0.8	5.221	(37)

Mechanism of action: With minimal impact on beta-2 receptors, metoprolol is a beta-1-adrenergic receptor inhibitor that is unique to cardiac cells. Without exhibiting intrinsic sympathomimetics or action towards membrane stabilization, this inhibition reduces cardiac output through adverse chronotropic and inotropic effects (7).

Need of analytical method development: The development and validation of analytical methods are ongoing, interrelated processes carried out during the drug development process. Establishing the suggested analytical method's accuracy, specificity, precision, and robustness for the pharmaceutical industry's analysis of a drug moiety is the main goal of its development and validation. The creation of a methodology is necessary for the pharmaceutical formulation's drug discovery, development, and assessment. Validation is required to demonstrate that an analytical method is appropriate and suitable for the intended use, which is frequently a crucial prerequisite for analytical purposes.(8)

Analytical method development by HPTLC: A more complex and automated version of thin-layer chromatography (TLC), high performance thin-layer chromatography (HPTLC) offers improved and more sophisticated separation efficacy and discovery limits. For routine sample analysis, a straightforward, precise, and accurate approach based on the HPTLC technology has been created. Additionally, the linearity, precision, delicateness, durability, and particularity of this system were confirmed. With a smaller mobile phase, a greater sample capacity, and numerous or regular times, the HPTLC method offers a number of advantages over other logical fashions (38).

Bioanalytical method development: The creation of a reliable bioanalytical method or methods is crucial to the drug research and development process, which ends with a marketing approval. Evaluation and interpretation of bioequivalence, PK, and toxicokinetic studies are greatly aided by bioanalysis, which is used to quantify medicines and their metabolites in biological fluids (48).

Table 3. Analytical Method Development Using HPTLC Method

S.No.	Sample	Stationary Phase/ Column	Mobile phase	Wavelength (nm)	Reference
1.	Tablet and bulk	Silica gel 60F254	Chloroform, methanol, ethyl acetate and formic acid (7.5:2.0:0.5:0.01, v:v:v:v)	227	(39)
2.	Tablet	Silica Gel G60 F254	Toluene: Chloroform: Methanol: Glacial acetic acid (45: 25: 25: 5 v/v/v/v)	231	(40)
3.	Tablet and bulk	Silica gel 60 F254	Chloroform: toluene: methanol: glacial acetic acid 6: 3: 1: 0.04 (v/v/v/v)	238	(41)
4.	Capsule	Silica Gel 60 F254	Methanol: Ethyl acetate: Triethylamine (6: 4: 0.1 v/v/v)	215	(42)
5.	Tablet and bulk	Silica gel 60F254	Toluene: ethyl acetate: methanol: triethylamine (4:1:1:0.4 v/v/v).	254	(43)
6.	Tablet and bulk	Method 1 - silica gel 60F254S Method 2 - RP-18 silica gel 60 F254S	Method 1 – Toluene: propanol: methanol: triethylamine (8: 1: 1: 0.5 v/v) Method 2 - Methanol: water: triethylamine (6: 4: 0.5 v/v)	242	(44)
7.	Capsule	Silica gel G 60 F25	Methanol-ethyl acetate-toluene-glacial acetic acid 2.5: 3: 4.5: 0.3 % v/v/v	224	(45)
8.	Tablet	Silica gel 60 F254	Methanol– ethyl acetate–water–toluene–25% ammonia 1.5:5.0:0.3:3.0:0.3 (v/v)	236	(46)
9.	Bulk	Silica gel F254	n-Butanol: Ethyl acetate: Triethylamine (6:4:0.1 v/v/v)	223	(47)

Table 4. Bioanalytical method development

S.No.	Method	Sample	Stationary phase/ column	Mobile phase	Wavelength (nm)	Flow rate (ml/min)	RT (min)	Reference
1.	UV-Spectroscopy	Tablet and plasma	-	50% Methanol	240.5	-	-	(49)
2.	LC-MS/MS	Tablet and human plasma	C18 column (50 mm × 2.0 mm, 3µm)	Acetonitrile and 0.5% formic acid (90:10 (v/v), pH 3.5)	-	0.2	1.34	(50)
3.	LC-MS/MS	Tablet and human plasma	C18 column, 33 mm × 4.6 mm, particle size 5 µm	Methanol–water containing 0.5% formic acid (8:2, v/v)	-	1.0	1.0	(51)

Analytical method development UV -Visible spectrophotometry: The analysis technique is based on detecting how much monochromatic light is absorbed by colorless substances in the 200–400 nm range of the near-ultraviolet spectrum. The processes required to ascertain the "identity, strength, quality, and purity" of such chemicals are included in the pharmaceutical analysis. It also covers the examination of intermediates and raw materials used in the production of pharmaceuticals. Light with a specific wavelength interval travel through a solvent-filled cell and lands on a photoelectric cell, which converts the radiant energy into electrical energy that can be measured by a galvanometer. This is the basic idea behind how a spectrophotometer covering the UV region works. The absorbance spectra of a substance in solution or as a solid are obtained using ultraviolet-visible spectroscopy (9).

Analytical method development by HPLC: High Liquid Chromatography Performance HPLC is a method of analysis used for solutes are separated according to their differences in elution rates inside a chromatographic column. The distribution determines this separation technique. between the mobile phase and the stationary phase. With HPLC, a substance can be identified. by trial and error as well as literature study. It is necessary to use a known chemical sample. to ensure that the unidentified component is identified (26).

CONCLUSION

The primary focus of this research has been the many analytical and bioanalytical techniques utilized to estimate the amount of metoprolol succinate present in different pharmaceutical products, both in bulk and in individual medications. The scientists have worked to create analytical and bioanalytical techniques, such as UV spectrophotometry, LC, HPLC, HPTLC, RP-HPLC, TLC, and other hyphenated techniques. Every analytical technique created has a higher degree of automation and sample throughput and is incredibly sensitive, dependable, reproducible, and exact. To gather data on various analytical instrumental approaches, a literature review is conducted. The development of a new analytical technique would benefit from such data.

Competing interest: The author has reported no conflict of interest in this article.

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