

ESTIMATION OF CLOPIDOGREL IN PHARMACEUTICALS-A REVIEW

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ABSTRACT

The main aim of this review article is to estimation of clopidogrel in pharmaceuticals by different analytical techniques. Also, this article tells on work done by various researchers' analysis on clopidogrel and in its combination of drugs. They used various stationary phases and mobile phases using different flow rates at appropriate detection wavelengths. Mostly used mobile phases are phosphate buffers and acetonitrile in combination and also with methanol. Stationary phase like Hypersil C18 column was used in almost all the works with the flow rates of 1ml/min. They have validated the methods according to ICH guidelines. This article highlights the clopidogrel estimation in single and combined dosage forms by various analytical techniques.

Keywords: clopidogrel, chromatography, flow rate, retention time

INTRODUCTION

Clopidogrel bisulphate is an antiplatelet agent or platelet aggregation inhibitor. The IUPAC name of clopidogrel bisulphate is Methyl (+) -(S)- α -(2-chlorophenyl)-6,7-dihydrothieno [3,2-c] pyridine-5(4H) acetate sulfate (**Figure 1**). The drug is practically insoluble in water at neutral pH, but freely soluble at pH 1. It is used to

inhibit blood clots in coronary artery disease, peripheral vascular disease, and cerebrovascular disease [1]. the drug is an irreversible inhibitor of the p2y12adenosine diphosphate receptor found on the membranes of platelets cells. Clopidogrel use is associated with several serious adverse drug reactions such as severe

neutropenia, various forms of hemorrhage, and cardiovascular edema [2]. Clopidogrel is chemically related to ticlopidine with superior side effects profile and dosing requirements. The drug which reduces platelet aggregation is extensively used for prevention of thrombosis in patients undergoing placement of a coronary stent [3]. Analytical methods for the determination of clopidogrel include mostly chromatographic and spectrophotometric techniques: high-performance liquid chromatography (HPLC), liquid chromatography, LC-MS/MS, LC-ESI-MS/MS, Super critical fluid chromatography (SFC), high-performance thin-layer chromatography (HPTLC), UV spectrophotometry. Furthermore, the determination of clopidogrel and its impurities by capillary zone electrophoresis was reported [4].

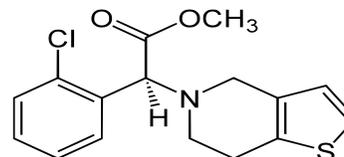


Figure 1: Clopidogrel

METHODS FOR ESTIMATION

UV Spectrophotometric methods

Various UV spectrophotometric methods for clopidogrel are listed in the (Table 1).

Chromatographic methods:

Various chromatographic methods like HPLC, HPTLC, SFC, was developed for estimation of clopidogrel. Methods for estimation Of HPLC and HPTLC, SFC are listed in the (Table 2).

Hyphenation techniques: Various hyphenation techniques like LC-MS/MS, HPLC-MS/MS, LC-ESI-MS- MS, Capillary zone electrophoresis (Table 3).

Table 1: Methods for estimation of clopidogrel by UV Spectrophotometry

S.no	Drugs	Method	Application	Description	Reference
1.	Clopidogrel	Spectrophotometry	Pharmaceuticals	Wavelength: 210,225nm Solvent: Acetonitrile Linearity range: 5-38 µg/ml	[5]
2.	Clopidogrel	Spectrophotometry	Pharmaceuticals	Detection wave length: 201-278nm Solvent: 0.1 N HCl, Methanol	[6]
3.	Clopidogrel	UV Spectrophotometric	Raw materials and pharmaceuticals	Detection wave length: 222nm Solvent: Distilled water Linearity range:40-70 µg/ml	[7]
4.	Clopidogrel	Spectrophotometric	In bulk and pharmaceutical preparation	Wave length: Cobalt thiocyanate: 625 nm Tpo00: 485 nm Solvent: 0.1M HCL, PH buffer solutions	[8]
5.	clopidogrel	UV Spectrophotometry	Raw material	Wavelength: 219, 225, 232, 237, 246nm Solvent: methanol	[9]
6.	Clopidogrel	Spectrophotometric	API	Wavelength: 256.0-287.2nm Solvent: chloroform	[10]
7.	Clopidogrel	Uv spectrophotometry	In bulk and its dosage form	Wavelength:218nm Solvent: Ethanol Linearity range: 2-12 µg/ml	[11]

Table 2: Methods for estimation of clopidogrel by HPLC

8.	Clopidogrel	HPLC	Pharmaceuticals	Detection wavelength: 235nm Mobile phase: 0.010 M NaH ₂ PO ₄ (pH 3.0): ACN (35:65 v/v) Column: Semi-micro column, BDS C8 (250×2.1 mm i.d., 5µm particle size) Flow rate: 0.30 ml/min Linearity range: 1.0-3.00 µg/ml Retention times: clopidogrel:3.08min Naproxen:6.28min	[12]
9.	Clopidogrel	HPLC	Pharmaceuticals	Detection wavelength: 220 nm Solvent: Methanol: KH ₂ PO ₄ (30 :70 v/v) Mobile phase: Acetonitrile Column: ABZ plus SUPELCO (250mm \square 4.6 mm i.d.) Flow rate: 1ml/min Linearity range: 10.0 to 90.0 µg/ml Retention time: clopidogrel:6.8 min	[13]
10.	Clopidogrel	RP-HPLC	In pharmaceutical dosage form	Detection wavelength: 220 nm Mobile phase: methanol: water {pH adjusted to 3.5 with 0.1% Acetic Acid} (95:05, v/v) Column: C ₁₈ ODS Flow rate: 1.0 ml/min Linearity range: 10-100 µg mL ⁻¹ Retention time: Diazepam:3.39min Clopidogrel:4.41min	[14]
11.	Clopidogrel	Stability indicating HPLC	Pharmaceuticals	Detection wavelength: 235 nm Solvent: 0.01 M Na ₂ HPO ₄ (pH 4): ACN (80:20 v/v) Mobile phase: Column: C-18 column Flow rate: 0. ml/min Linearity range: 0.2-3.5 µg/ml Retention time: clopidogrel:6.84min	[15]
12.	Clopidogrel	HPLC-UV	Pharmaceuticals	Detection wavelength: 220 nm Mobile phase: MeOH: Phosphoric acid 25 mM (80:20 v/v) Column: Hypersil BDS RP C18 (250 × 4.6mm, 5 µm) Flow rate: 1 ml/min Linearity range: 0.005-5.0 µg/ml Retention time: Diclofenac sodium:4.15min Clopidogrel:4.62min	[16]
13.	Clopidogrel	RP-HPLC	In bulk and pharmaceutical dosage forms	Detection wavelength: 224 nm Mobile phase: Acetonitrile: phosphate buffer = 60:40 v/v Column: C ₁₈ Flow rate: 1.0 ml/min Retention time: 9.182min	[17]

14.	Clopidogrel	RP-HPLC	Pharmaceuticals	Detection wavelength: 220 nm Mobile phase: Potassium dihydrogen orthophosphate buffer: ACN (32:68 v/v) Column: Hypersil BDS C18 (250 × 4.6 mm, 5 μm) column Flow rate: 1.0ml/min Linearity range: 50-150μg/ml Retention time: 3.847 min	[18]
15.	Clopidogrel	SFC	Pharmaceuticals	Detection wavelength: 215nm Mobile phase: Chiral cel OD-H – Mobile phase – supercritical fluid: 2- propanol Column: Chiral cel ODH column Linearity: 8-52 μg/ml Flow rate: 2 ml/min	[19]
16.	Clopidogrel	RPHPLC	Raw materials and pharmaceuticals	Detection wavelength:225nm Mobile phase: ACN: Phosphate (65:35 v/v) Column: Develosil ODS HG-5 RP C18 (15 cm × 4.6 mm, i.d. 5 mm) Flow rate:1ml/min Linearity range:10-60 μg/ml Retention time:7.48 min	[20]
17.	Clopidogrel	RPHPLC	Raw materials and pharmaceuticals	Detection wavelength:238nm Mobile phase: Phosphate Buffer: ACN (pH 3.0) (70: 30 v/v) Column: Thermo Hypersil RP C18 column (100 mm x 4.6 mm, 3.5 μm) Flow rate:1.0ml/min Linearity range: 10-60 μg/ml Retention time: 4.75min	[21]
18.	Clopidogrel	HPLC	Chemometric Assisted LC method	Detection wavelength: 210 nm Mobile phase: 0.1 % v/v trifluoroacetic acid: 0.1 % v/v phosphoric acid: 0.025M phosphate buffer Column: a Hypersil Gold, 5-μm 150 x 4 mm column Flow rate: ml/min linearity:0.125-100μg/ml	[22]
19.	Clopidogrel	HPLC	Wistar rat plasma	Detection wavelength: 220nm Mobile phase: Water: MeOH: ACN (40:40:20 v/v/v) Column: Kromasil ODS, 250 mm × 4.6 mm i.d., 5 Flow rate: Linearity range: 125.0– 32,000 ng mL ⁻¹	[23]
20.	Clopidogrel	HPLC	Human serum	Detection wavelength: 220 nm Mobile phase: Water: 0.05 M phosphate buffer (containing TEA 0.5 mL L ⁻¹ - pH 5.7): ACN (56:44 v/v) Column: Shimpack CLC-ODS (150 mm × 4.6 mm i.d: 5 μm protected by Shimpack G-ODS guard column (1 cm × 4.0 mm i.d: 5 μm) Flow rate: 0.9 ml/min	[24]

				Linearity range: 0.05 – 10µg /ml-1	
21.	Clopidogrel	HPLC	Human serum	Detection wavelength: 220 nm Mobile phase: TEA (0.5 mL L - 1 pH 5.7): ACN (56:44 v/v) Column: C ₁₈ Column temperature: 50 Flow rate: 0.9 ml/min Linearity range: 0.05-10 µg mL ⁻¹	[25]
22.	Clopidogrel	HPTLC	In bulk and pharmaceutical dosage forms	Detection wavelength: 230nm Mobile phase: carbon tetrachloride-chloroform- acetone (6:4:0.15, v/v/v). Stationary phase: TLC aluminium plates precoated with silica gel 60F-254 Retardation factor: clopidogrel: 0.30 Linearity range: 200-1000 ng per spot	[26]
23.	Clopidogrel	HPTLC	In pharmaceutical dosage forms	Detection wavelength: 254nm Mobile phase: hexane: methanol: chloroform: ammonia (16:2:1.5:0.5, v/v/v/v) Stationary phase: aluminium plates precoated with silica gel 60F-254 Retardation factor: clopidogrel: 0.65	[27]

Table 3: Methods for estimation of clopidogrel by Hyphenation techniques

24.	Clopidogrel	LC-ESI-MS- MS	Human plasma	Detection wavelength:220nm Mobile phase: Water: MeOH: ACN (40:40:20 v/v/v) Column: Zorbax SB C-18 (75 mm x 4.6 mm x 3.5 µm) Agilent Flow rate:0.3ml/min Linearity range: 25 to 25.0 ng mL ⁻¹ for SR25990C and 50.0 to 6000.0 ng/ml for SR26334	[28]
25.	Clopidogrel	Capillary Zone Electrophoresis	Human plasma and urine	Mobile phase: Uncoated Silica capillary filled with phosphate buffer (pH 2.5) Column: Fused silica capillary, 35 cm × 50 m i.d: 26.5 cm Linearity range: 0.25 – 20.0 mg L ⁻¹ in plasma and 0.25 – 10.0 mg L ⁻¹ in urine	[29]
26.	Clopidogrel	Capillary Zone Electrophoresis	Human plasma	Mobile phase: Uncoated Silica capillary filled with phosphate buffer (pH 2.5) Column: Fused silica capillary, 35 cm × 50 m i.d: 26.5 cm Linearity range: 2 – 100 µm	[30]

27.	Clopidogrel	LC-MS/MS	Human plasma	Detection wavelength: m/z - 308.10 - 113 Mobile phase: Diethyl ether: n-Hexane (80:20 v/v) Column: C18 column Flow rate: 0.5 ml/min Linearity range: 25 – 3000 ng mL ⁻¹ Retention time: 1.82 min	[31]
28.	Clopidogrel	Potentiometry	Human (serum-urine)	Detection Wavelength: 215 nm Mobile phase: distilled water linearity: 1.0 x 10 ⁻⁷ - 1.0 x 10 ⁻² mol L	[32]

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CONCLUSION

Finally, I conclude that this article emphasis on the clopidogrel and its combination of drugs by different analytical techniques. This article encloses the work done on clopidogrel by adopting various methods with different analytical instruments. In near future, it would be helpful for the researcher who wants to carry out his/her work on clopidogrel. By validating the all the developed methods, I came to a conclusion that estimation of clopidogrel can be carried out in routine laboratory scale.

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