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# A REVIEW ON ESTIMATION OF CLOPIDOGREL AND ASPIRIN IN BULK AND IN PHARMACEUTICAL DOSAGE FORM

**Dhanshri R. Shinde*, Dr. R. B. Laware, Dr. S. B. Dighe and Ankita V. Deodhe**

Department of Pharmaceutical Quality Assurance and Technology, Pravara Rural College of Pharmacy, Pravaranagar. Tal-Rahata, Dist.-Ahmednagar.

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***Corresponding Author**
**Dr. Dhanshri R. Shinde**
Department of Pharmaceutical Quality Assurance and Technology, Pravara Rural College of Pharmacy, Pravaranagar. Tal-Rahata, Dist.-Ahmednagar.

## ABSTRACT

Platelet activation and aggregation are considered to be central to arterial thrombus formation. Antiplatelet therapy is therefore important for both the treatment and prevention of cardiovascular disease. The literature has revealed that number of method have been published for estimation and of clopidogrel and aspirin like RP-HPLC, Spectrophotometric (UV), UPLC, etc. These methods were reported for analysis. The review gives information of development and validation of clopidogrel and aspirin in bulk and pharmaceutical dosage form and validation as per ICH guidelines. thise is a fixed drug combination available in these generation. These drugs are compatible with other antiplatelate drug which having same or equal potency and less side effect.

**KEYWORDS:** Clopidogrel, aspirin, analytical method.

## INTRODUCTION

The antiplatelet therapy for prevention of thrombotic events in cardiovascular disease are evident. Statistical studies have shown that secondary prevention prevention by antiplatelet agent reduces risk of myocardial infraction and stroke.[1]

Clopidogrel is used to reduce the risk of heart disease and sroke in those at high risk. it is also together with aspirin in heart attacks and following the placement of a coronary artery.[2]

**MECHANISM OF ACTION**

Aspirin is the most widely used antiplatelet agent which inhibites platelet cyclo-oxygenase and the conversion of arachidonic acid to the potent platelet agonist thromboxane A but not prevent platelet activation occurring via various signaling pathways that are independent of thromboxane A release. Therefore a number of other compounds have been developed to complement aspirins beneficial effect. these includes thiopyridines like clopidogrel.[3]

Aspirin irreversibly inhibits cyclo-oxygenase in platelet and therefore blocks the formation of thromboxane A and the clopidogrel is metabolized in liver to its active compound which covalently bind to the adenosine phosphate receptor on platelet and dramatically reduces platelet aggregation. Clopidogrel is a prodrug, which is activated in two steps, first by CYP2C19, CYP1A2 AND CYP2B6, then by CYP2C19, CYP2C9, CYP2B6 and CYP3A steps. The active metabolite then specifically and irreversibly inhibits the P2Y12 subtype of ADP receptor, which is important in activation of platelet and eventual cross linking by the protein fibrin. Platelet inhibition can be demonstrated two hours after a single dose of oral clopidogrel but the onset of action is slow, so a loading dose either 600 or 300 mg is administrated when a rapid effect is needed.[2]

**DRUG PROFILE**

**ASPIRIN**

IUPAC Name : Acytyl salicylic acid or 2-acetoxy benzoic acid

Moleculer formula : C9H8O4

Moleculer weight :180.159 g/mol

Physical Description: Oderless white crystalline powder with a bitter taste

Boiling point : 140 °C

Melting point : 135 °C

Category : Antiplatelet and anti imflamatory agent

Solubility : Soluble in methanol and slightly Soluble in water

**CLOPIDOGREL**

IUPAC name : Methyl(2S)-2(2-(chorophynyl)-2-(6,7-dihydr -4h-thieno[3,2-c]pyridine-5-yl)acetate.

Molucular formula : C16H16CINO2S

Molecular weight : 321.82 g/mols

Physical description :solid colorless powder.

Melting point : 158°Cs

Category :Platelet aggregation inhibitors.

**PHARMACOKINETIC DATA**

**Aspirin**

Route of administration : by orally (tablets)

Protein binding : 50-80% in bood to albumin protein.

Metabolism : 80% aspirin is metabolized in liver.

Elimination half life : 15 -30 hours.

Excretion : By renal excretion.[8]

**Clopidogrel**

Route of administration : By orally (tablets)

Protein binding : Human plasma protein 98-94%

Metabolism : By liver

Elimination half life : 0.5-1 hours

Excretion :By renal excretion [2]

**Reported Analytaical Method**

| Title | Method | Discription |
|---|---|---|
| [4] Concurrent estimation of clopidogrel and aspirin in tablet dosage form | RP-HPLC | Column: Phenomenex Luna C18<br>M.P.:Acetonitrate, potassium Dihydrogenphosphate, Buffer methanol (50:30:20v/v)<br>Wavelenght : 240 nm<br>Flow rate :1.5 ml/min<br>Retantion time : 10 and 9 min.<br>Detector: Diode array detector. |
| [5]Simultaneous estimation of aspirin and clopidogrel in combine tablet dosage form | RP-HPLC | Column: Kromasil HD C18<br>M.P.: Acetonitrile and 0.1%v/v Orthoporic acid aquous Solution(40:60v/v)<br>Wavelenght: 237nm<br>Flow rate:1.5 ml/min<br>Retantion time:4.9<br>Detector: Diode array detector |
| [6]Method development and validation of aspirin and clopidogrel | RP-HPLC | Column :AC18 column<br>M.P.: Acetonitrate and pottasium buffer (40:60v/v) |

| | | |
|---|---|---|
| | | Wavelenght: 224nm<br>Flow rate:1ml/min<br>Retantion time: 9.1<br>Detector: Photo diode array Detector |
| [7]Analysis of aspirin and clopidogrel in combination | RP-HPLC | Column: phenomenex C18<br>M.P: Acetonitrile, methanol And phosphate buffer (50:7:43 v/v)<br>Wavelenth: 240nm<br>Flow rate: 1ml/min<br>Retantion time: 9.2 and 10<br>Detector: photo diode array |
| [8]Simultaneous Determination of Clopidogrel and Aspirin from Bulk Material and Dosage Formulations Using Multivariate Calibration Technique | RP-HPLC | Column : C18 reversed Phase Analytical column<br>M.P.: Methanol ,water (80,20v/v)<br>Wavelenth: 225nm<br>Flow rate : 1ml/min<br>Retantion time: 3.2 and 6<br>Detector: photo diode array |
| [9]Simultaneous determination of Aspirin and Clopidogrel bisulphate in Tablet and Capsule Dosage Form | Ion pairing RP-HPLC | M.P.:a)water and methanol (80:20v/v)<br>b)Acetonitrile and water (50:50)<br>Wavelenth : 240 nm<br>Resolution : 6.09<br>Retention time:3 and 5.7min.<br>Flow rate :0.8 and 1 ml/min. |
| [10]A Validated Stability Indicating HPTLC Method for Determination of Aspirin and Clopidogrel Bisulphate in Combined Dosage Form | HPTLC | Solvent : carbon tetrachloride-Aceton chloride (6: 2.4 v/v). TLC Stationary phase :aluminum plates precoated with silica gel 60 F254<br>Retantion factor:0.13 and 0.78<br>Presaturation : 20 min. |
| [11]Simultaneous estimation of aspirin and clopidogrel in pharmaceutical dosage form | HPTLC | Solvent :Methanol<br>Stationary phase :TLC plate Percolated with silica Gel<br>M.P.:Tolune,Methanol, Chloroform (5:3:2)<br>Wavelenth: 226nm |
| [12]Method development and validation of aspirin and clopidogrel in APIs and its pharmaceutical dosage form | LC | Column :ODC Devosil C18<br>M.P.: buffer and cetonitrile (65:35v/v)<br>Wavelenth : 229nm |

| | | |
|---|---|---|
| | | Flow rate : 1ml/min<br>Retention time :2.6 and 3.6 |
| [13]Validated bio-analytical method development for simultaneous estimation of clopidogrel and aspirin in human plasma | UFLC | Column: phenomenex C18<br>M.P. :Phosphate buffer and Acetonitrile (35:65v/v)<br>Flow rate :1.5 ml/min<br>Retantion time :2.5 and 5.3 min<br>Wavelenth :230 and 252nm<br>Run time :10 min. |
| [14]Simultaneous Estimation of Clopidogrel and Aspirin in Capsule Dosage forms with third constituent is Atorvastatin | UV-SPECROSCOPY | Wavelenth:ASP-235nm<br>CLO-220nm<br>ATR-247nm<br>LOD: ASP- 0.67<br>CLO- 0.67<br>ATR- 0.12<br>LOQ: ASP- 2.1<br>CLO- 2.9<br>ATR- 0.37 |

## CONCLUSION

Thise review study is basic aproch for the RP-HPLC, HPLC, LC, UFLC AND UV spectroscopic analytical method of analysis of aspirin and clopidogrel bisulphate in bulk and tablet dosage form the different chromatographic parameter are used in respective method which result in diffrences in resolution time. This help in determining the selection of optimum chromatographic parameter such as cheaper mobile phase with lesser resolution time. Aspirin and colpidogrel are available in combination as well as single drugs with less side effect. As recent literature reviews, suggest that there are only few method reported for simultaneous estimation of aspirin and clopidorel by RP-HPLC method was optimized and validated as per ICH guidelines.

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