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DIFFERENT ANALYTICAL TECHNIQUES FOR THE ANALYSIS OF ANTICANCER DRUGS - ERLOTINIB, GEFITINIB, PONATINIB - A REVIEW

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ABSTRACT

In this present situation increase in the number of diseases has been observed and several medications were provided to treat the diseases, which are approved by FDA. But before these drugs come to the market the drug must be validated by several procedures which help in ensuring its purity and reliability. This process uses to collect data about the drug. This review includes various types of analytical method and techniques such as UV spectrophotometric and some chromatography methods, hyphenation techniques such as LC-MS of the drugs have been discussed.

KEYWORDS: Analytical techniques, UV-spectrophotometric, LC-MS.

1. INTRODUCTION

Analytical techniques like titration, spectroscopic techniques, chromatography and gravimetric analysis are developed to test the specific characteristic of the substance against the pre-defined acceptance criteria for such characteristics. Thus, analytical method development involves the evaluation and selection of most precise assay procedure to determine the composition in drug. This method used to determine a chemical or physical property of a chemical substance, chemical elements or mixture of compounds. Analytical method development, validation and transfer are key factor.[1]

FDA

An agency of FDA is founded on 30 June 1906, and head-quarters at Silver Spring, Maryland, united states. Founders were Theodore Roosevelt, Harvey Washington Wiley. The United state and food and drug administration is federal agencies of the department of health and human service. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco product, dietary supplements, and prescriptions over the counter pharmaceutical drugs, vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting device, cosmetics, animal foods and feeds and veterinary products. The FDA's primary focus is enforcement of the federal food, food and cosmetic act, but the agenise also enforces the other lose, notably section 361 of the public health service act, as well as associated regulations. Much of this regulatory / enforcement work is not directly related to food or drugs but involves such things as regulating lasers, cellular phones and condoms, as well as control of diseases in contact varying from households pets to human sperm donate for use in assisted reproduction.[2]

2. Analytical methods

UV Spectrophotometric

It considered as most traditional instrumental system of analysis and UV spectrometric is a finest method used for determining analyte which are present in sample and in semi micro & micro amounts. UV concerned with detection of the effects of electromagnetic radiation interacting with absorbing entities such as molecules, ions or atoms. UV spectrometric method is useful for analysing the various substances such as organic compounds, inorganic compounds and bimolecular. Result of this analyte are used for research purpose, clinical trial laboratories, industry, UV also helpful for environmental samples therefore UV is necessary to learn about the origin of the UV-VIS spectrum and its characteristics.[3]

HPLC

High performance liquid chromatography is a process of separating components in a liquid mixture. A liquid sample is injected into a stream of solvent (mobile phase) flowing through a column packed with a separation medium (stationary phase). HPLC is that leading distinctive separating instrument it is used for many aspects of analysis and drug manufacture. As high-performance liquid chromatography is specific and highly sensitive it gives precise result. But high-performance liquid chromatography is widely used for two reasons firstly analysis and qualitative of unknown mixtures and secondly mixture separation for the later analysis.

The separation mode depends totally on interacting relationship between the mobile phase, analyte and stationary phase.[4-5]

LC/MS-MS

The LC/MS-MS is considered as most potent analytical process which is specific and sensitive. The LC-MS is hyphenated analytical system which works in combination of two system mass spectrometry and liquid chromatography. Via passing throughout the column the components of mixture get separated in HPLC, but this LC cannot differentiate the separated compounds so, MS helps to identify unknown substances and also useful to elucidate their structures. As, spectrum mixture is highly complicated because of overlapping spectra, MS individually is not helpful for identifying mixtures. Hence, they are used in combination for more exact result. Therefore LC/MS-MS is possible to separate and molecule masses at the same time are determining relative atomic masses.[6-7]

Table 1: A summary of different analytical methods used for the estimation of selected anti-cancer drugs.

S. No	Brand Name	API	Analytical Method	Description of the Method	Reference
01	Traceva	Erlotinib	RP-HPLC	**System:**Water's 2695 Milford, USA with UV detector **Column:** Merk C_{18} (250 cm X 4.6mm) **Mobile Phase:** Potassium dihydrogen Phosphate 0.02M : Acetonitrile (70:30V/V) **Wavelength:** 246nm **Flow rate:** 0.8 ml/min: **Linearity Range:** 10-60µg/ml **Retention time:** 4.54 min **LOD:** 6.62 µg/ml **LOQ**: 20.07 µg/ml	[8]
			HPLC	**System:**Water's 2695 Milford, USA with PDA detector. **Column:** Kromarin 100-5 C_{18} (150mmX4.6mm I.D, 5µM) **Mobile Phase:** Buffer**:** Acetonitrile: Methanol (65:21:14 V/V) **Flow rate:**1.5ml/min	[9]

				Injection volume: 10µl **Wavelength:** 250nm **Run time:** 15 min **Linearity:**75.02µg/ml-225.06µg/ml **Retention time:** 8.259 min	
			HPLC	**System:**Knauer HPLC(Berlin, Germany) **Column:** ODS inertsil (150 mmX4.6mm,3.5µ) **Mobile phase:** Methanol: Acetonitrile:Potassium dihydrogen phosphate buffer (15:45:40% V/V) **Wavelength:**332nm **Flow rate:**1.3ml/min **Linearity:** 320-20000 ng/ml **Run time:** 6 min **LOD:** 46 ng/ml **LOQ**: 150 ng/ml	[10]
			HPLC-UV	**System:**Water's 2695 Milford, USA with UV detector **Column:** Merk C_{18} (250 cm X 4.6mm) **Mobile phase:** Acetonitrile: 20mM ammonium acetate pH 4.5 **Flow rate:** 0.4 ml/min **Run time:** 15 min **Wavelength:**331nm **Linearity:**80-4000ng/ml	[11]
02	Iressa	Gefinitib	HPLC-UV	**System:** Water's 2695 Milford, USA with UV detector **Column:** Merk C_{18} (250 cm X 4.6mm) **Mobile phase:** Acetonitrile: 20mM ammonium acetate pH 4.5 **Flow rate:** 0.4 ml/min **Run time:** 15 min **Wavelength:**331nm **Linearity:**80-4000ng/ml	[11]
			HPLC-DAD	**System**: HPLC-DAD **Column:**C_{18} column gradient elution **Mobile phase:** 0.1% Triethyl amine solution: Acetonitrile **Wavelength:**344nm	[12]

				Injection volume:CSF:0.11ng/ml plasma:11ng/ml	
			RP-HPLC	**System:** Agilent HPLC **Column:**Agilent[4.6X250mm] **Mobile phase:**Trifluro acetic acid [0.1%]: Methanol [35:65] **Injection volume:**10µl **Wavelength:**246nm **Flow rate:**1ml/min **Retention time:**3.8min **Linearity:**5-30µg/ml **LOD:** 1.481µg/ml **LOQ:** 4.48930µg/ml	[13]
			RP-HPLC	**System:**LC 10 AT-VP with PDA detector (Shimadzu-Japan) **Column:** Inertsil ODS-$_3$V **Mobilephase:**130mM Ammonium acetate: Acetonitrile (63.37V/V) **Flow rate:**1.0ml/min **Linearity:**0.1-2.0µg/ml **Wavelength:**260nm **LOD**: 0.033µg/ml **LOQ**: 0.10µg/ml	[14]
			LC-MS/MS	**System:**HPLC **Column:** X terra RP$_{18}$ Column[50X2.1mm,3.5µm **Mobile phase:**Water:Acetonitrile[35:65V/V] **Run time:**3min **Flow rate:**0.35ml/min Linerity: 0.5-1000 ng/ml	[15]
			RP-HPLC	**System**: Shimadzu Model CBM-20A/20 Alite HPLC system with PDA detector **Column**: Agilent C18 column **Mobile phase**: Tetra butyl ammonium hydrogen sulphate: Methanol (50:50 v/v) **Detection wavelength**: 340 nm **Linearity**: 10-80 µg/mL	[16]

				LOD: 0.2931 µg/mL **LOQ**: 0.8947 µg/mL	
			SPECTROFLUORIMETRIC	**Solvent**: Ethanol **Excitation wavelength (λmax)**: 280 nm **Emission wavelength (λmax)**: 512 nm **Linearity** : 1-3.5 µg/mL **LOD**: 0.0299 µg/mL **LOQ**: 0.0906 µg/mL	[17]
03	ICLUSIG	Ponatinib	HPLC	**System:**LC20AD,Shimadzu, Kyoto,Japan with UV detector-SPD-20A **Column:** Capcell pack C_{18} MGII[25X4.6mm] **Mobile phase:** Acetonitrile: 0.037mol/L KH_2PO_4[pH4.5] [39:61V/V] **Wavelength:**250nm **Flow rate:**1.0ml/min **Linearity:**5-250 ng/ml **LOQ:** 5 ng/ml	[18]
			LC-MS/MS [Human plasma andrat liver microsomes]	**System:** Agilent-HPLC-MS/MS(6410 QqQ) **Column:** Agilent eclipse plus C_{18} [50mmX2.1mm,1.8µm] **Flow rate:**0.25ml/min^{-2} **Run time:**4min **Mobile phase: Solvent A** [10mM Ammonium format pH adjusted to 4.1 with Formic acid]:**Solvent B** - Acetonitrile **Mass spectrometric detector:** Ions were generated by electrospray (ESI) and multiple reaction monitoring [MRM] was used as basic for quantification **Linearity:**5-400ngmL^{-2} **LLOQ:**4.66ngmL^{-1} in plasma, 4.19ngmL^{-1} in RLMs	[19]

Table 2: Brand names for anticancer drugs.[20]

Si. No.	API	Brand name	Manufacturing company
1	Erlotinib	Erlocip (150)	Cipla limited
		Lortinib (150)	Rpg life science ltd
		Erlova (100)	Glenmark pharmaceutical. Ltd
		Erlotec (150)	United biotech pv. Ltd.
2	Gefitinib	Iressa	astrazeneca pv. Ltd
		Chemofit	Rpg life sciences ltd
		Gefires	Resonance laboratories pvt. Ltd
		O-gnat (250)	Sain medicaments pvt. Ltd
		Gefticare (250)	Medicare remedies pvt. Ltd.
3	Ponatinib	Iclusig	Aiad pvt. Ltd
		Ponaxe	Everest pharm ltd.

3. CONCLUSION

The development of analytical method is essential for developing the any pharmaceutical products. Analytical method development and validation are continues and inter connected activities throughout the drug development process The practice of validation refers that the given method measuring parameter and establish the performance limits of the measurements the result are drug development and define the emerging knowledge base supporting the product although many validation parameter for particular drug it is concluded the various analytical technique like spectrophotometric, HPLC, LC-MS/MS, RP-HPLC, HPLC-UV, HPLC-DAD can be further developed for this formulation with the variation**.**

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