International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

Development of Impurity Profiling Methods Using Modern Analytical Techniques

Bhaumik R. machhi[1]*, Vaidehi Panchal[2], Prof.Mitali Dalwadi[3], Dr. Umesh Upadhyay[4]

[1]*VII[th] Semester B.Pharm, Sigma Institute of Pharmacy, Bakrol, Ajwa, Vadodara, (390019) Gujarat, India*
[3]*Assistant Prof. Sigma Institute of Pharmacy, Bakrol, Ajwa, Vadodara, (390019) Gujarat, India*
[4]*Principal, Sigma Institute of Pharmacy, Bakrol, Ajwa, Vadodara, (390019) Gujarat, India*

Date of Submission: 1-11-2020 Date of Acceptance: 15-11-2020

ABSTRACT: The review provides temporary introduction concerning method and merchandise connected impurities and Emphasizes on the event of novel analytical ways for his or her determination. It describes application of recent analytical techniques, notably the UPLC, LC-MS, HRMS, GC-MS and HPTLC.additionally, to that the appliance of resonance (NMR) spectrographic analysis was additionally mentioned for characterization of impurities and degradation product. The importance of quality, effectuality and safety of drug substance/products together with the supply of impurities, kinds of impurities; adverse effects by the presence of impurities, control of impurities, necessity for development of impurity identification ways, identification of impurities and regulative aspects were mentioned.

Keywords: Impurity identification, Stabilityindicatingassayways,HPLC,GC,HPTLC,UPLC,NMR,LC-MS,GC-MS,Chrometography,trendy analytical techniques.

I. INTRNODUCTION

The pharmaceutical trade is associate degree integral a vicinity of world's economy these days. The trade has been created and can continue build an oversized impact on human life. one among the key areas of focus for pharmaceutical industries is R & D sector to develop new drug molecules. It spends ~1000 million greenbacks and takes 10-15 years to develop a replacement drug molecule. Duringthe 10 years amount from 2010 to 2020, the agency approved over 280 therapeutic new molecularentities thus, the management on the standard, safety and effectuality of those medicines is veryimportant issue to the regulative authoritiesFrom the last decade, analytical support for the drug discovery and development processhas intense. As a result, new technologies square measure unceasingly evolving to fulfill these challenges. Today, pharmaceutical analysis is employed to supply precise and correct knowledge, to not solely supportdrug discovery and development however additionally post market police investigation. Developing analyticalmethod for recently introduced drug substance or formulation could be a matter of most importance. to ascertain the standard standards of the medication totally different analytical techniques like titrimetric, spectrophotometric, qualitative analysis, and activity techniques square measure used. Nowadays, pharmaceutical analysis plays a awfully crucial role in making the premise for development of extremely economical drug therapies by providing analytical input to artificial, medical specialty, pharmaceutical and clinical analysis. Particularly, quantification of impurities, degradation product and drug dose could notbe official in any accumulation and therefore, analytical technique for determination could notavailable. These impurities square measure the key culprits of the poor quality of medication. analysis of the and potential impurities could be a crucial activity in drug development method. Hence, thespectroscopic studies (e.g., NMR, IR and MS) ought to be conducted to characterize the structureof actual impurity or degradation product gift among the drug substance. The apparent levels of0.1% or higher than, impurities ought to be scientifically even. this review topic was selected supported the increasing wants of thepharmaceutical trade in developing appropriate analytical ways. Among the many otheravailable techniques, the fashionable analytical techniques like UPLC, LC-MS, LC-Q-TOF, GCMS, HPTLC and LC- NMR were mentioned. additionally,

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

thereto the supply of impurities, types ofimpurities; management of impurities, identification of impurities, regulative aspects, degradationproducts and stability indicating assay ways (SIAMs) were mentioned (2)

II. IMPORTANCEOF MORDEN ANALYTICAL TECHNIQUES TO DETERMINE IMPURITIES.

Until the start of twentieth century, medicines were made and marketed with no management over purity and safety. At that point quality of the foremost of medication were poor and proprietary with dubious price. For instance, teratogen could be a downer introduced within the early Nineteen Sixties. This caused serious malformation in newborn babies of ladies UN agency consumed throughout youth of maternity. Thereafter, it had been known that the s-enantiomer of teratogen possessed agent action and has no power for the desired sedative property.(1) Thereupon, the Food, Drug, and Cosmetic act (FD&C) was revised requiring advance proof of safety and a number of {other and several other} other controls for brand spanking new medication. The simplest example to elucidate the requirement for development impurity identification strategies is pain pill. In 1970s, its quality was tested by titrimetric assay victimization us, British and Indian assemblage. (3) A color check was enclosed in book, used for detection of free hydroxy acid as a degradation product. Once HPLC become well-liked in pharmaceutical analysis, additionally to hydroxy acid, 3 a lot of impurities were found in bulk drug substances.it absolutely was found that these impurities area unit reacting with supermolecule amino functions that area unit to blame for allergies.(4) Hence, subtle equipment's area unit necessary for pharmaceutical analysis particularly in impurity identification. Out of all analytical techniques, the action techniques like HPLC, UPLC and LC-MS have gained prime importance.

III. IMPORTANT METHODS FOR DETRMINIG THE IMPURITY.

HPLC: -

High-performance liquid chromatography formerly referred to as high-pressure liquid chromatography, is a technique in analytical chemistry used to separate, identify, and quantify each component in amixture.

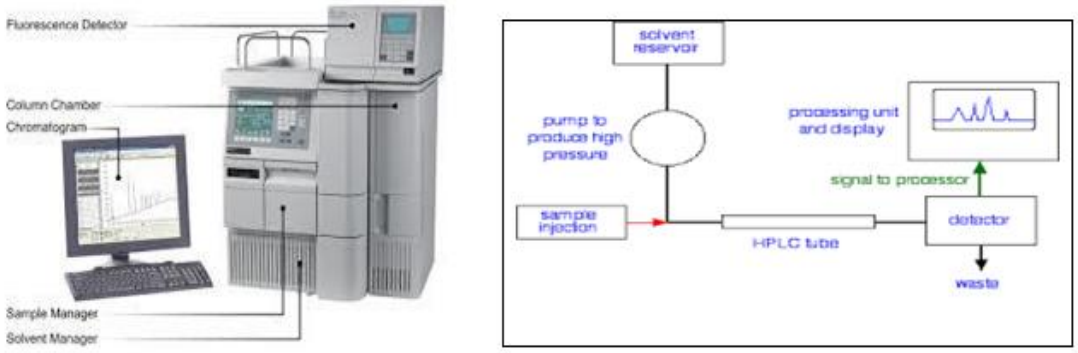

FIGURE NO: -1WORKING DIAGRAM OF HPLC

HPLC is most widely used analytical technique because it is non-destructive and applied to thermally liable compounds also (unlike GC). Many unique column packing (stationary phase) and wide choice of detection techniques are available to provide a huge range of selectivity for separation. Reverse phase liquid chromatography (RPLC) is more widely used because of its broad selectivity, reproducibility, compatibility with pharmaceutical samples, and its suitability for MS detection .In most of the cases, revers\ed phase (C18, C8 etc.) columns and UV and PDA detectors are preferred for HPLC analysis detection also useful in checking purity of chromatographic peaks.(5,6,7)

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

UPLC: -

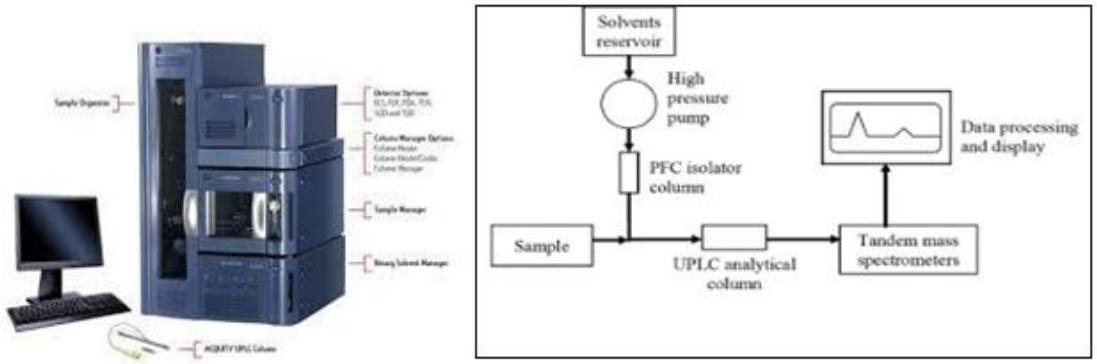

FIGURE NO: -2WORKING DIAGRAM OF UPLC

UPLC is a modern technique which gives a new Direction for liquid. chromatography. UPLC refers to ultra-performance liquid chromatography, which enhance mainly in three areas: "speed, resolution and sensitivity.Ultra-Performance liquid chromatography (UPLC) is that the successor technology to HPLC Techniques since the 1970s. UPLC provides similar analytical efficiency as that of HPLC but Operates at much higher pressures. The most of HPLC columns contains particles size in between 2.5 to 5 microns. While UPLC columns was developed based upon sub 2-micron porous particles. These require a higher pressure ~15,000 psi in order to obtain high flow rates as compared to particles in HPLC column (< 6000 psi). (8)Due to the small size of the particles, the diffusion path between the stationary phase and analyzes is shorter and the efficiency is higher. Conceptually, the sensitivity of the UPLC detection has 2-3 times higher than HPLC detection, depending on the detection technique used. Due to significant advances in instrumentation and column technology were made to realize prominent increases in speed, resolution and sensitivity in UPLC. Hence, UPLC make them ideally fitted to use with mass spectrometry and it's a crucial drive in today's pharmaceutical industry.(9,10)

HRMS: -

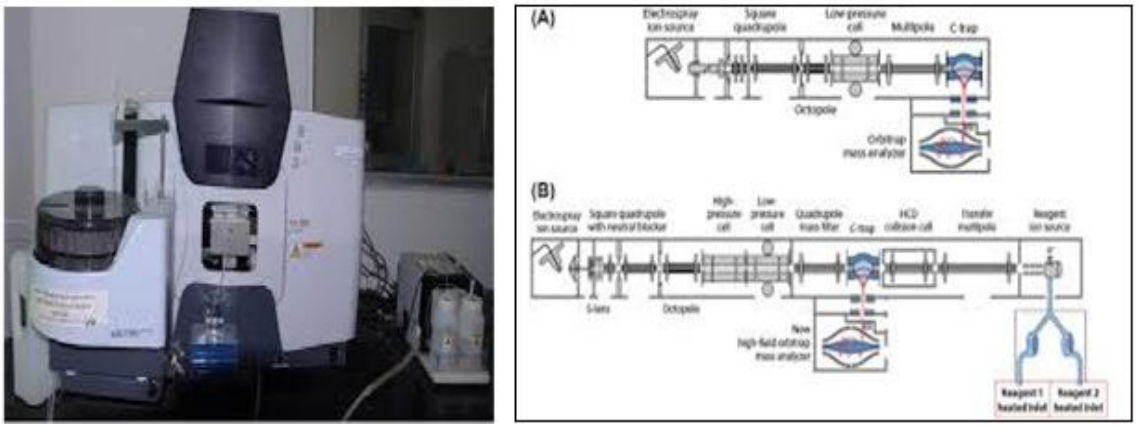

FIGURE NO-3 WORKING DIAGRAM OF HRMS

High-resolution mass spectrometry: Mass spectrometry in which m/z for each ion is measured to several decimal places (i.e., exact masses are measured, instead of nominal masses).Particularly useful to differentiate between molecular formulas having the same nominal masses. High-resolution MS (HRMS) is rapidly advancing into many fields of modern analytical sciences. It provides information associated with the relative molecular mass, elemental composition, and molecular structure of a compound. It can also be used to perform tandem mass spectrometry

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

(MS/MS) experiments to obtain more fragmented ions. After identification of functional groups or moieties in the fragmented ions are used to assemble for the prediction of structureof a molecule. HRMS can determine m/z values accurately up to four decimal places. TOF analyzer not only provides accurate mass measurements but also establish probable formula of an unknown compound. Since a given nominal mass may correspond to many molecular formulas, lists of such possibilities are especially useful when evaluating the spectrum of an unknown compound. Composition tables are available for this purpose, and a particularly useful program for calculating all possible combinations of H, C, N & O that give a specific nominal mass. HRMS is especially useful in metabolomics, to compute not just the elemental composition but even the isotopic ratios of unknown species. HRMS instruments have resolution within the range of about 10,000 and up to the millions.(14,15)

GC-MS: -

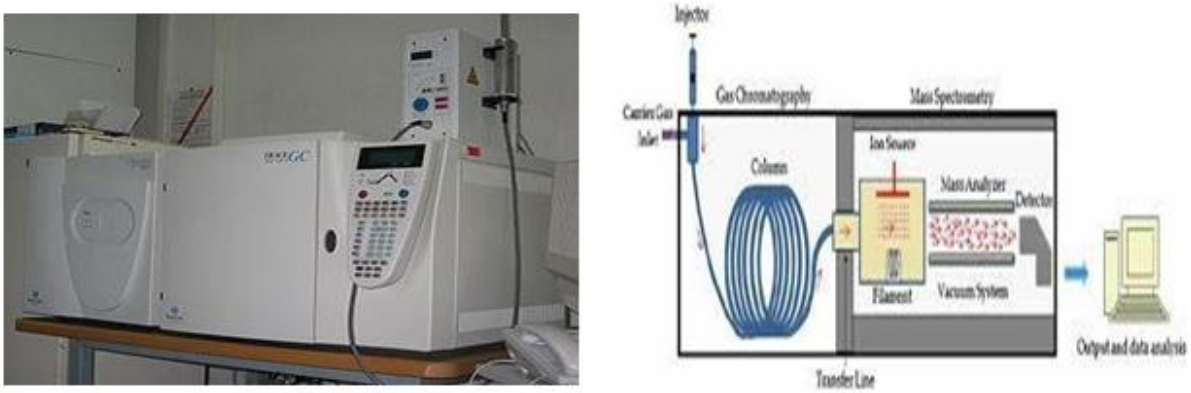

FIGURE NO: -4 WORKING DIAGRAM OF GC-MS

Gas Chromatography-Mass Spectrometry (GC-MS) may be a hyphenated analytical technique that's want to separate volatile, semi volatile compounds, residual solvents and thermally stable, compounds. The separation mechanism depends difference in the boiling points the separation occurs in column. Then the separated components enter into the MS through an interphone. This is followed by ionization, mass analysis and detection of m/z ratios of ions generated from each analysis taken place. Two widely used Ionization techniques in GC-MS are the electron impact ionization (EI) and chemical ionization (CI) in either positive or negative modes. The main advantage of GC-MS is that the mass spectra show a selected pattern like compounds. Therefore, the comparison of a measured spectrum to a database is an efficient identification method. GC-MS is additionally a crucial tool for identification, characterization of medicine and drug metabolites, stability testing, analysis of impurities in pharmaceuticals, analysis of pesticides and herbicides, quantization of pollutants in drinking and wastewater, oils in creams, ointments, lotions etc. The main advantage of GC-MS is that the mass spectra show a selected pattern like compounds. Therefore, the comparison of a measured spectrum to a database is an efficient identification method. GC-MS is additionally a crucial tool for identification, characterization of medicine and drug metabolites, stability testing, analysis of impurities in pharmaceuticals, analysis of pesticides and herbicides, quantization of pollutants in drinking and wastewater, oils in creams, ointments, lotions etc.(15,16)

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

HPTLC

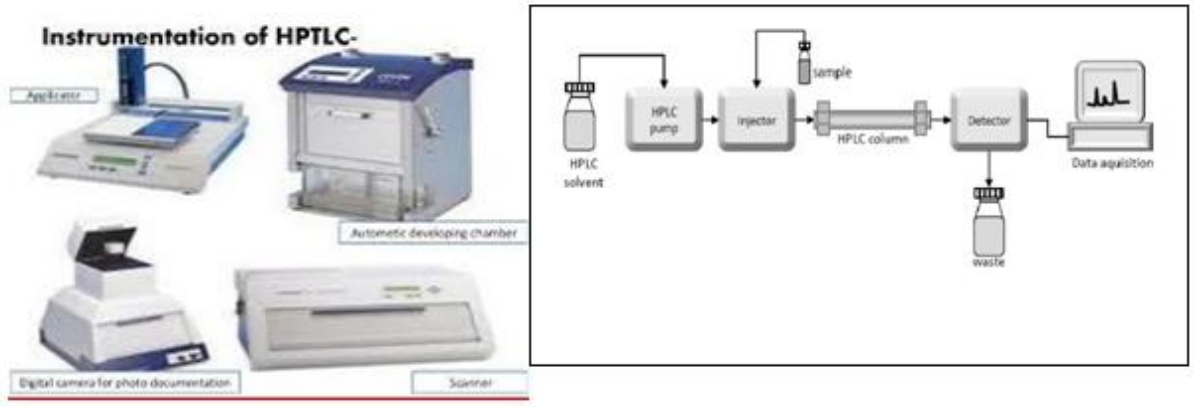

FIGURE NO: -5 WORKING DIAGRAM OF HPTLC

HPTLC could also be a contemporary adaptation of TLC with better and advanced separation efficiency and detection limits. HPTLC is that the only chromatographic method offering the choice of presenting the results as a picture . Other advantages include simplicity, parallel analysis of samples, low costs, rapidly obtained results, and possibility of multiple component detection.HPTLC method may help to minimizes exposure risk of toxic organic effluents and significantly reduces its disposal problems. HPTLC remains increasingly finding its way in pharmaceutical analysis with the advancements within the introduction of densitometers as detection equipment and therefore the stationary phases. HPTLC is one among the foremost widely applied methods for the analysis in pharmaceutical industries, forensic chemistry, clinical chemistry, biochemistry, food and drug analysis, cosmetology, environmental analysis, and other areas.(17,18,19).

NMR: -

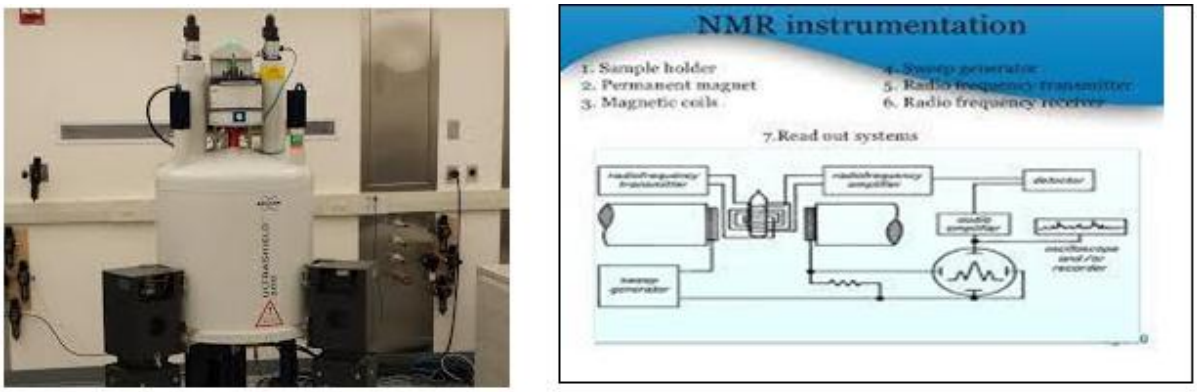

FIGURE NO: -6 WORKING DIAGRAM OF NMR

NMR spectroscopy exploits the magnetic properties of certain atomic nuclei. It determines the physicochemical properties of atoms or molecules during which they're contained. Structural elucidation of impurities in drug substance/product mostly involves the appliance of 1H and 13C NMR spectroscopy. additionally, the two-dimensional experiments like double quantum filtered correlation spectroscopy (DFC-COSY), and hetero nuclear single quantum coherence (HSQC) also are useful in structure elucidation of organic molecules. the mixture of chromatographic separation techniques with NMR spectroscopy (LC-NMR) offers advantages for the on-line separation and structural elucidation of unknown compounds. The advancements in pulse field gradients, the development in probe technology, solvent suppression, and therefore the construction

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

of high field magnets are the driving forces to the present technique. Mixtures like crude reaction mixtures in drug discovery are often analyzed without prior separation. However, LC-NMR wasn't widely practical because of its low sensitivity. LC-NMR provide complementary information about structures simultaneously and offer a way for more accurate and rapid structural analysis. Specifically, interfacing liquid chromatography with parallel NMR and mass spectrometry (LC–NMR–MS) gives comprehensive structural data on metabolites of novel drugs in development. of these analytical techniques are wont to assess the standard, efficacy and safety of pharmaceutics. (20,21,22).

LC-MS

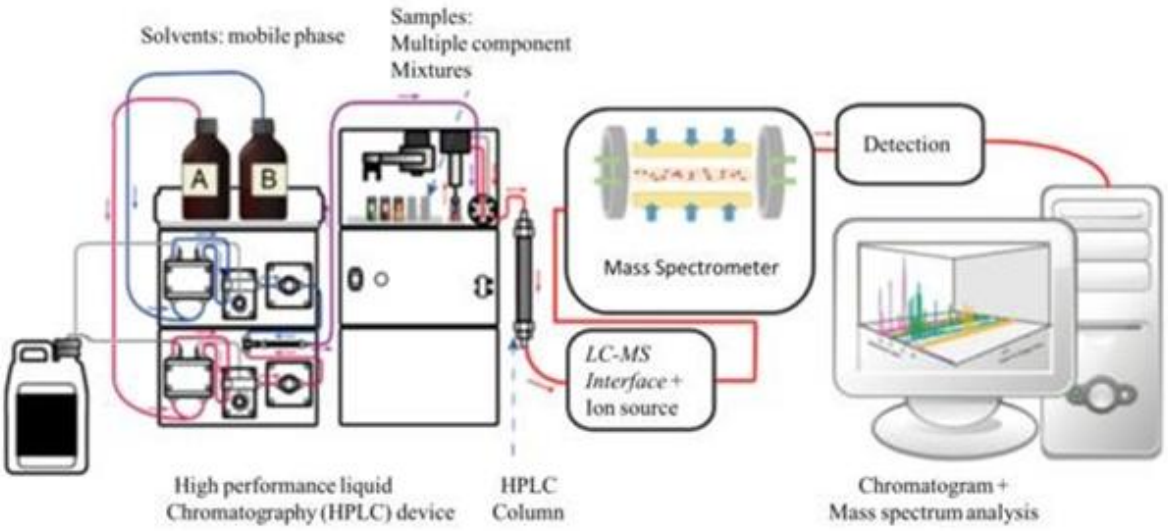

FIGURE NO: -6 WORKING DIAGRAM OF LC-MS

Liquid chromatography-mass spectrometry (LC-MS) may be a powerful tool for identification and structural characterization of organic molecules in various matrices. It generates mass spectral data which will produce valuable information about the relative molecular mass, identity, quantity, purity and structure of a sample. It can analyze compounds that have lack of suitable chromophore, which isn't possible by LC-UV/PDA for analysis. Hence, it are often considered as a universal detector for analysis of pharmaceutical samples. It also can wont to identify components in unresolved chromatographic peaks and reducing the necessity for desired separation. Thus LC-MS found an area in every drug development activity right from research to toxicology studies. (11) Several ionization techniques are developed over the years depending upon the state and nature of sample. During the ionization process, the analytes are converted into fragment ions and which may be used for subsequent analysis on the idea of their mass to charge ratio (m/z). The main ionization methods include electron impact (EI), atmospheric pressure chemical ionization (APCI), electrospray ionization (ESI), matrix-assisted laser desorption/ionization (MALDI), chemical ionization (CI) and fast atom bombardment (FAB). Out of which ESI and APCI techniques have been using frequently in drug development and analysis.

The electrospray ionization (ESI) technique was developed by John Fenn for analysis of biological macromolecules. It is utilized in mass spectrometry to supply ions using an electrospray during which a high voltage is applied to a liquid to make an aerosol. ESI is that the soft ionization technique and most ordinarily employed in LC-MS analysis, during which the molecular ion always observed.

Another advantage of ESI is that solution-phase information are often retained into the gas-phase. However, limited structural information obtains from the sample mass spectrum.(12) This disadvantage are often overcome by coupling ESI with tandem mass spectrometry (ESI-MS/MS). Atmospheric pressure chemical ionization (APCI) is another soft ionization technique and therefore the ionization of the substrate is efficient. It utilizes gas phase ions and molecule reactions

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

atatmospheric pressure. It is mainly used for polar and relatively non-polar compounds with a molecular weight of polar and relatively non-polar compounds with a molecular weight of <1500 Da. Generally, it produces monocharged ions because of its ability to run in sequence with LC. Due to which, it has gained immense popularity in pharmaceutical analysis. A potential advantage of APCI is that it is possible to use a no polar solvent as a mobile phase instead of a polar solvent. This technique is useful for small and thermally stable molecules that are not well ionized by ESI. For example, free steroids do not ionize well singes because they are neutral and relatively non-polar molecules. (13,14)

IV. TYPES OF IMPURITIES

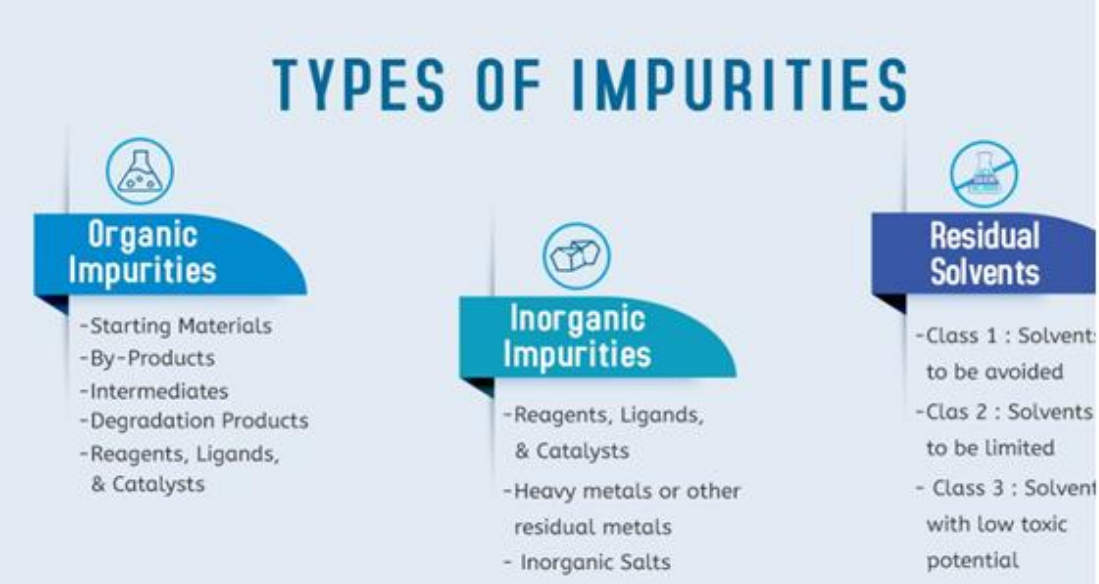

FIGURE NO: -7 TYPES OF IMPURITY

ORGANIC IMPURITIES: -

- Organic impurities could arise throughout the producing method and/or storage of the drug substance. they are derived from drug substance artificial processes and degradation reactions in drug substances and drug product. artificial method connected impurities square measure typically derived from beginning materials, intermediates, reagents, ligands, and catalysts used within the chemical synthesis, additionally as by-products from the side-reactions of the chemical synthesis. Degradation product square measure derived from the chemical degradation of drug substances and drug product beneath storage or stress. conditions. they're going to be known or unidentified, volatile, or non-volatile, and embody the next A) Impurities Originating from Drug Substance artificial Processes: Most little molecule drug substances square measure with chemicals synthesized. Chemical entities, other than the drug substance, that square measure concerned or created at intervals the artificial method square measure typically carried over to the last word drug substance as trace level impurities. These chemical entities embody raw materials, intermediates, solvents, chemical reagents, catalysts, by-products, impurities gift at intervals the beginning materials, and chemical entities fashioned from those beginning material impurities (particularly those concerned at intervals the last steps of the synthesis). These impurities square measure typically mentioned as method impurities. The goal of method impurity identification is to figure out the structures and origins of these impurities. this information is important for up the artificial natural action, thus on eliminate or minimize method impurities.(23,24)

Orginic Impurities In Raw Materiales

- Impurities gift within the staring materials might follow an equivalent reaction pathway because the beginning material itself, and therefore the reaction product might carry over

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

to the ultimate product as method impurities. information of the impurities in beginning materials helps to spot connected impurities within the final product, and to know the formation mechanisms of those connected method impurities. One such example is that the presence of a 4-trifluoromethyl point compound in 3-trifluoromethyl-a-ethylbenzhydrol (Fiumicino), because of the presence of 4-trifluoromethylbenzeneimpurity within the beginning material, 3-trifluoromethylbenzene. A second example involves a 2-methyl analogue gift as a trace impurity in tolperisone, because of the presence of 2- methyl group propiophenone within the beginning material, 4-methylpropiophenone.(25,26)

Reagents, Ligands and Catalysts:

- These chemicals are less normally found in APIs; but, in some cases they will create a tangle as impurities. Chemical reagents, ligands, and catalysts used within the synthesis of a drug substance ar usually carried over to the last word product as trace level impurities. as an example, acid chloromethyl tetrahydro-pyran-4-yl organic compound (CCMTHP), that is used as Associate in Nursing alkylating agent inside the synthesis of a ß lactam drug substance, was ascertained inside the ultimate product as Associate in Nursing impurity. several chemical reactions are promoted by metal-based catalysts. as Associate in Nursing example, a Ziegler-Natta catalyst contains metallic element, Grubb¨s catalyst contains metallic element, and Adam¨s catalyst contains noble metal. In some cases, reagents or catalysts might react with intermediates or final product to form byproducts. Pyridine, a catalyst used within the course of synthesis of mazipredone, reacts with Associate in Nursing intermediate to form a pyridinium impurity. (27)

➢ **INORGANIC IMPURITIES: -**

RAW MATERIALES

- Pharmaceutical substances square measure either isolated from natural sources or synthesized from chemical beginning materials that have impurities. Impurities associated with the raw materials might even be carried through the producing method to contaminate the last word product.

FROM MATHOS OF MANUFACTURE:

- (A)Reagents used at intervals the producing process: -Calcium carbonate contains 'soluble alkali' as impurity Anions like Cl - then four -2 square measure common impurities in several substances because of the use of acid associated sulphury acid severally metal particle might even be an impurity in peroxide
- (B) Regents need to eliminate alternative impurities: metal is utilized to induce eliminate sulfate from salt, which can be found itself (barium) as impurity at the highest of method.
- (C)Solvents:
- tiny amounts of solvents used in preparation, and purification of the merchandise also can finish within the contamination of the pharmaceutical substances. half-dozen book of facts of Inorganic Impurities in prescription drugs.
- (2) Water is that the most cost effective solvent which can be the most supply of impurities as a result of it contains totally different kind of impurities like Ca 2+, Mg 2+, Na +, Cl -, CO3 -2 then four -2 in trace amounts(28,29)

Impurity Present In Marketed Drug And Methods Use For Purify It.

TABLE NO-1(30)

S.R NO	DRUGS	Impurities	METHOD
1	Amphotericin B	Tetraenes	UV spectroscopy
2	Atropine sulphate	Apo atropine	UV spectroscopy
3	Cloxacillin	N, N -dimethyl	Gas chromatography
4	Dextrose	5- hydroxy methyl furfural	UV spectroscopy
5	Doxorubicin hydrochloride	Acetone and Ethanol	Gas chromatography
6	Ethambutol hydrochloride	2 -amino butanol	TLC

International Journal of Pharmaceutical Research and Applications
Volume 5, Issue 2, pp: 423-434www.ijprajournal.com ISSN: 2249-7781

7	Fluorescence sodium	Dimethyl formamide	Gas chromatography
8	Framicetinsulphate	Enamine	TLC
9	Morphin	6- mono ichthyomorphic	HPLC
10	10-hydroxymorphin	10- oxomorphin	HPLC
11	Mercaptopurin	Hypoxanthin ,2,5-bis*(N' cyano–N''–methyl) guinidinoethylthiomethyl]-4-methylimidazol	UV spectroscopy
12	Norgestrei	3,17a-diethyl-13ethyl-3,5-gonadiene-17-ol spectroscopy	TLC, HPLC and UV
13	Cimitidine	1,8-bis*(N'cyano-N''-methyl)guinidino]-3,6-dithiaoctane	HPLC
14	Celecoxib	5-(4-methylphenyl)-3trifluromethyl-1H-pyrazole],4-[5(2'- methylphenyl)-3(trifluromethyl-1H-pyrazole-1-yl]benzenesulphonamide,and4[4-(4'-methyl phenyl)-3-(trifluromethyl)-1Hpyrazole-1-yl]benzenesulphonamide	HPLC, LC, LC-MS-MS
15	Ethynodioldiacetate	17 a-ethinylestr-4-ene-3a,17-diol-3-acetate-17-(3'-acetoxy-2'-butenoate)17 a-ethinylestr-4-ene-3a,17-diol-3-acetate-17-(3-oxobutanoate)	HPLC
16	Methamphetamine	1,2-dimethyl-3-phnylaziride,ephedrine,methylephedrine,N-formylmethamphetamine,N-acetylmethamphitamine,,N-formylphedrine,N-acetylephedrine, N,Oacetylephedrine,methametamine dimmer	HPLC
17	Repaglinide	4-carboxymethyl-2-ethoxybenzoic acid,4-cyclohexylaminocarbamoylmethyl-2ethoxy-benzoic acid,1- cyclohexyl-3-[3-methyl-1-2-(piperidine-1-ylphenyl)-butyl]-urea,1,3-dicyclohexyl urea	GC
18	Morphine	6-monoacetylmorphine	HPLC
19	Morphine sulphate	5-(hydroxymethyl)2-furfural	HPLC
20	10-hydroxymorphine	10-oxomorphine	HPLC

V. APPLICATION OF DIFFERENT ANALYTICAL METHODS FOR REMOVINGIFFRENTIMPURITIES.

HPLC

- High performance liquid activity (HPLC) is routinely used for determination every|of every} assay and impurities in each bulk active and developed drug product. Impurity profile analyses unit required to demonstrate the ability to note a wide vary of impurities which can occur in pharmaceuticals.(31)

GC-MS

- Gas activity is additionally a physical separation technique in where volatile mixtures unit separated. It unit usually utilized in many alternative fields like pharmaceuticals, cosmetics and even environmental toxins.The identification of impurities in industrial Sudan III was performed by GC/MS combined with trimethylsilylation (TMS).
- a full of twenty four impurities were known or tentatively characterized in industrial Sudan III dyes by GC/MS and were chiefly classified as

phenylazo and naphtholazo analogs. Four new impurities with two-dimensional structures, suspected of being virulent compounds, were discovered in industrial Sudan III dyes. For a lot of identification and sensitive detection of polar impurities, academic degree extract was trimethylsilyl- derivatized to spice up the speed action properties and mass qualitative analysis detection sensitivity. (32)

HPTLC

- A superior thin-layer action technique (HPTLC) has been developed for the determination then the purity management of a artificial fluoroquinolone antibiotic antibiotic compound in coated tablets once desfluoro compound, alkene chemical compound compound, by- compound A and fluoroquinolonic acid unit thought of as impurities. mixture F254 was used as a stationary half and a mix of acetonitrile, ammonia twenty fifth, wood spirit and chloride (1:2:4:4, v/v/v/v) as a mobile half.
- The arrange of action was valid in terms of spatiality (range), property (placebo and connected compounds), precision, accuracy (Recovery), system suitability (repeatability, peak symmetry, resolution) and impurities limit of detection (LOD). The analysis of variance (ANOVA) and t-test were applied to correlate the results of antibiotic compound determination in coated tablets by means of the HPTLC technique then the official British assortment (BP 1999) superior liquid action (HPLC) technique.(33)

NMR

- Nuclear Magnetic spectrometry (NMR) is that the most powerful technique for determinant the structure of organic compounds. magnetic resonance techniques square measure used with success in varied food systems for internal control and analysis. magnetic resonance spectrometry is employed to see structure of proteins, amino acid profile, carotenoids, organic acids, lipide fractions, the quality of the water in foods.
- Magnetic resonance spectrometry is additionally accustomed determine and quantify the metabolites in foods. additionally, vegetable oils, fish oils, fish and meat, milk, cheese, wheat, fruit juices, coffee, green tea, foods like wine and brew square measure among the last magnetic resonance applications. additionally, magnetic resonance spectrometry is employed for food omics that may be a new discipline that brings food science and organic process analysis along. magnetic resonance techniques used for the food authentication square measure one- and two-dimensional magnetic resonance techniques, high resolution liquid state 1H and 13C magnetic resonance techniques, N15 and P-31 magnetic resonance techniques, 1H HR/MAS (high resolution magic angle spinning) magnetic resonance techniques. At this study, usage functions of nuclear resonance spectrometry for foods were collected. (34)

UPLC

- An analytical technique for determination of the active substance diclofenac, the degradation product 1-(2,6-dichlorphenyl)-2-indolinone, and so the preservatives methylparaben and propylparaben was used for testing and scrutiny LC systems. varied octadecylsilica-based analytical columns were examined. Acquity UPLC BEH C18 (2.1 x 50 mm, 1.7 microm) and (2.1 x 100 mm, 1.7 microm) were tested for UPLC.(36)

LC-MS

- Pharmaceuticals want careful and precise determination of their impurities which might hurt the user upon consumption. the' lately, the foremost common technique for impurities identification is liquid chromatography- mass spectroscopic analysis (LC- MS/MS), it's several downsides because of the character of the ionization technique. (35)

VI. CONCLUSION

This review describes role of recent analytical techniques, particularly UPLC, LC-MS, LC-Q-TOF-MS, GC-MS and HPTLC. additionally, thereto the appliance of nuclear resonance (LC-NMR) spectroscopy was also discussed for characterization of impurities and degradation products. the importance of quality, efficacy and safety of drug substance/products including the source of impurities, sorts of impurities; adverse effects by the presence of impurities in drug substance/product, control of impurities, necessity for development impurity profiling methods, identification of impurities, regulatory aspects and its internal control were discussed.

REFRENCE

[1]. Ronald Bentley From Optical Activity in Quartz to Chiral Drugs: Molecular Handedness in Biology and Medicine Perspectives in Biology and MedicineJohns Hopkins University PressVolume 38, Number 2, Winter 1995pg. 188-229.

[2]. Bondigalla Ramachandra. DevlopmentOf impurity Profiling Method Using MordenAnalytical technique Critical Reviews In Analytical Chemistry, Volume 47,27Jun 2016.

[3]. W.J.Irwin,Q.N.MasudaA,Li Wan Po.Transesterification: An analytical and formulation problem. Journal of Pharmaceutical and Biomedical Analysis,Volume 3, Issue 3, 1985, Pages 241-250.

[4]. A,VerstraetenE.RoetsJ,Hoogmartens.Quantitative determination by high-performance liquid chromatography of acetylsalicylic acid and related substances in tablets. Journal of Chromatography A.Volume 388, 1987, Pages 201-216.

[5]. Hani Naseef , 1Ramzi Moqadi , and MoammalQurt . Development and Validation of an HPLC Method for Determination of Antidiabetic Drug Alogliptin Benzoate in Bulk and Tablets. Journal of Analytical Methods in Chemistry. Volume 2018, 23 Sep 2018.

[6]. Snyder. L.R, Kirkland. J.J, Glajch. J.L. Practical HPLC Method Development, 2nd edition, John Wiley & Sons, Inc., New York, 1997, 233-264.

[7]. Veronika R. Meyer.High-Performance Liquid Chromatography (HPLC). Practical Methods in Cardiovascular Research. pg661-685.

[8]. Hamid Khan, Javed Ali. UHPLC: Applications in Pharmaceutical Analysis. Asian J. Pharm. Ana. 2017;Vol- 7, Pg-124-131.

[9]. VijayRam,GovindKher,KapilDubal,Bhavesh Dodiya,HitendraJoshi. Development and validation of a stability indicating UPLC method for determination of ticlopidine hydrochloride in its tablet formulation.Saudi Pharmaceutical Journal.Volume 19, Issue 3, July 2011, Pages 159-164.

[10]. Nikalje Anna Pratima, Baheti Shraddha, Sayyad Zibran.Review of Ultra Performance Liquid Chromatography and Its Applications. International Journal of Research in Pharmacy and Science.Vol-3,pg 19-40,2013.

[11]. Mike. S. L. LC/MS applications in drug development. John Wiley & Sons, Inc.NewYork,Vol-1,2002.

[12]. Sharma Devanshu, Mittal Rahul, Gupta Annu, Singh Kishan, Nair Anroop. Quantitative Bioanalysis by LC-MS/MS: A Review. JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES. Vol- 07, Issue 07.2010.

[13]. Vivek K. Vyas,Manjunath,Ghate,RaviUkawala. Recent Advances in Characterization of Impurities - Use of Hyphenated LC-MS Technique. Current Pharmaceutical Analysis.Vol -6 pg-299-306 Nov2010.

[14]. David J. Harvey ,Robert H. Bateman. High- energy Collision- induced Fragmentation of Complex Oligosaccharides Ionized by Matrix- assisted Laser Desorption/Ionization Mass Spectrometry. JOURNAL OF MASS SPECTROMETORY.Vol-32, issue no 2pg-167-187 December 1998.

[15]. Kataria Sahil, Beniwal Prashant, Middha Akanksha, Sandhu Premji, Rathore Devashish. GasChromatography-Mass Spectrometry: Applications. International Journal of Pharmaceutical & Biological Archives.Vol-2 issue no-6, pg- 1544-1560, 29 Oct 2011.

[16]. Ashish Chauhan, Manish Kumar Goyal, Priyanka Chauhan GC-MS Technique and its Analytical Applications in Science and Technology. Journal of Analytical & Bioanalytical Techniques.Vol-5, November 17, 2014.

[17]. Sonia, k & Shree, B.S. & Lakshmi, K.S.. . HPTLC method development and validation: An overview. Journal of Pharmaceutical Sciences and Research.Vol-9.pg- 652-657.2017.

[18]. Koll, Kathrin & Reich, Eike & Blatter, Anne &Veit, Markus. Validation of Standardized High-Performance Thin-Layer Chromatographic Methods for Quality Control and Stability Testing of Herbals. Journal of AOAC International.Vol-86. Pg-909-15,2003.

[19]. Mahesh Attimarad, K. K. Mueen Ahmed, Bandar E. Aldhubaib, and Sree Harsha. High-performance thin layer

chromatography: A powerful analytical technique in pharmaceutical drug discovery.Pharm Methods.Vol-2, Issue-2, pg-71–75,2011.

[20]. Lee. Griffiths.Optimization of NMR and HPLC Conditions for LC-NMR. Anal. Chem.Vol-67, issue no 22, pg-4091–4095,1995.

[21]. Corcoran, Olivia &Spraul, Manfred. LC-NMR-MS in drug discovery. Drug discovery today-Vol 8.pg-624,2003.

[22]. Ulrike Holzgrabe, Myriam Malet-Martino. NMR Spectroscopy in Pharmaceutical and Biomedical Analysis. Journal of Pharmaceutical and Biomedical Analysis. Vol-93, Pages 1-160, May 2014.

[23]. Poonam Kushwaha. Organic Impurities present in Pharmaceuticals and Food Products. Pharmaceutical Reviews. Vol. 6 Issue 4 ,2008.

[24]. Qiu, F. and Norwood, D.L., Identification of pharmaceutical impurities, journal of liquid chromatography & related technologies, vol.30, page no. 877-935,2007.

[25]. Roy. Jiban.Pharmaceutical impurities – A mini review. AAPS Pharm SciTech vol.3, no2, 2000.

[26]. Gorog.sandor. chemical and analytical characterization of related organic impurities in drugs.AnalBioanal. Chem, vol.377, 2003, pp. 852-862,2003.

[27]. Gavin, P.F. & Olsen, B.A. A quality evaluation strategy for multi-sourced active pharmaceutical ingredient (API) starting materials. J. Pharm. Biomed. Anal. , Vol-41 issue-4, 1251–1259,2006.

[28]. Muehlen, E. Impurities in starting materials and drugs. Pharmazeut. Ind. Vol-54 issue-10, 837–41,1992.

[29]. Shukla, Parjanya& Verma, Amita. Handbook of Inorganic Impurities in Pharmaceuticals.2014.

[30]. Shreya R. Shah*, Mayur A. Patel, Miral V. Naik, P.K. Pradhan, and U.M. Upadhyay. RECENT APPROCHES OF "IMPURITY PROFILING" IN PHARMACEUTICAL ANALYSIS: A REVIEW. International Journal of Pharmaceutical Sciences andReserch.Vol 3, pg 3603,2012.

[31]. Timothy W. Ryan. HPLC Impurity Profile Analyses of Pharmaceutical Substances Using UV Photodiode Array Detection. Analytical Letters, Vol- 31 Issue-4, pg - 651-658,1998.

[32]. Ji YeonHonga,NaHyunParkaKyung ,HoYoobJongkiHong. Comprehensive impurity profiling and quantification of Sudan III dyes by gas chromatography/mass spectrometry.Journal of Chromatography.Volume 1297, Pages 186-195, 5 July 2013.

[33]. PrawezAlam ,EssamEzzeldin,Muzaffar Iqbal ,Gamal A.E. Mostafa ,Md. Khalid Anwer 5,Mohammed H. Alqarni 1,Ahmed I. Foudah 1 andFaiyaz Shakeel. Determination of Delafloxacin in Pharmaceutical Formulations Using a Green RP-HPTLC and NP-HPTLC Methods: A Comparative Study. Volume 9, Issue 6,25 June 2020.

[34]. Parlak Y, Güzeler N. Nuclear Magnetic Resonance Spectroscopy Applications in Foods. Curr Res Nutr Food Sci Vol-4, October 2016.

[35]. Svetlana Tsizin,AvivAmirav. Analysis of impurities in pharmaceuticals by LC- MS with cold electron ionization.Journal of mass spectrometroy.Vol-55,Issue-10, 11 June 2020.

[36]. Nováková, Lucie &Solichová, Dagmar &Solich, Petr.Advantages of ultra performance liquid chromatography over high-performance liquid chromatography: Comparison of different analytical 2 approaches during analysis of diclofenac gel. Journal of separation science.vol-29 issue-16,2433-43.2006.