A Review on Spectroscopic analytical method validation and force degradation study.

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Abstract: A basic, exact, precise, and explicit and RP-HPLC technique was produced for assurance of medication in drug detailing. The introduced investigation is straight forward, since tests are straight forwardly utilized with no fundamental synthetic sensation or then again cleaning advances. For the most part a RP-HPLC examine use Evenness C18 or proportionate with versatile stage arrangement of ph 7 cradle: acetonitrile [40:60] was utilized, and stream rate was 0.8 ml min-1 with UV discovery at 285 nm. The proposed technique was approved for different ICH boundaries like linearity, cutoff of discovery, exactness, accuracy, toughness, strength, what's more, framework reasonableness

Keywords: Force Degradation, RP-HPLC, Validation.

1 Introduction

Analysis is vital in any product or service, and it is also important in drug because it involves life [1]. Analytical chemistry is the analysis of separation, quantification and chemical additives identification of herbal and synthetic materials constituted with one or more compounds or factors. Analytical chemistry is separated into two predominant classes, a qualitative evaluation that is to say the identification with regard to the chemical additives exists in the sample, whereas quantitative evaluation estimates the amount of positive detail or compound within the substance, i.e. the sample [2]. The quantity of medication brought into the marketplace is growing each year. These medicines could also be either new entities or partial structural alteration of the present one. Medicines ought to be accessible in such a type that quality as well as bioavailability, adequate plasma concentration, desired period, the onset of action, correct dose, safety, effectiveness and stability on storage of product, will be assured throughout the storage of the products [3]. The advancement of a medication is a long procedure including drug invention, a research lab trial, preclinical testing, clinical testing, and regulatory registration. To additionally improve the adequacy and protection of the medication after acceptance, numerous administrative organizations, for example, the united states food and drug administration (USFDA) likewise require that the drug product is evaluated for its identification, potency, characteristics, quality, stability, and purity before it can be discharged for utilizing. Thus, pharmaceutical validation and process controls are vital in disregarding the issues that might be encountered [4]. Frequently, there is a time lag from the date of introduction of a medication into the market to the date of its consideration in pharmacopeias. This occurs because of the possible vulnerabilities within the continuous and more extensive use of those drugs, reports of ongoing toxicity (bringing about their withdrawal from the market), development of affected person resistance and improvement of higher medicine with the aim of competition. Under these situations, requirements and analytical techniques for those medicines that may not be approachable within the pharmacopoeias. It becomes necessary, so as to develop newer analytical strategies for such medications [5]. Analytical approach improvement and validation perform important functions in the discovery, improvement, and manufacturing of medications. The main aim of an analytical measure is to get consistent, realistic, and correct information. Validated analytical strategies play a significant role in achieving this goal. Outcomes from methodology validation may be used to choose the standard, reliability, and consistency of analytical results, that is associated as an integral part of any sensible analytical practice. Validation of analytical strategies is also needed by most rules and quality standards that impact laboratories [6].

1.1 Analytical method development

When there are no definitive techniques are present, new methodologies are being progressed for evaluation of the novel product. To investigate the presence of either pharmacopoeial or non-pharmacopoeial product novel techniques are developed to reduce the value besides time for higher precision and strength. These methodologies are optimized and valid through preliminary runs. Alternate ways are planned and place into practice to exchange the present procedure within the comparative laboratory information with all accessible merits and demerits.

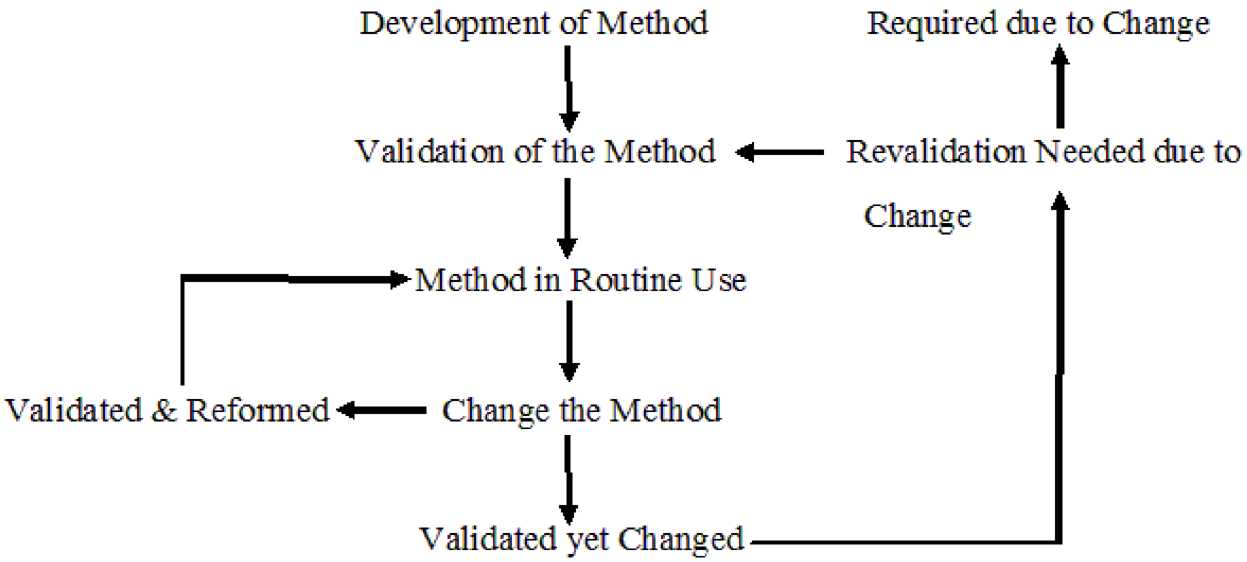

Figure 1: Life cycle of the analytical method [7]

1.1.1 Necessity of method development

Drug evaluation exhibits the identity characterization and resolution of the drugs in combination like dosage forms and organic fluids. At some point of producing technique and development of drug the principal purpose of analytical strategies is to generate data regarding efficiency (which might be directly connected with the need of a identified dose), impurity (related to safety of the medication), bioavailability (consists of key drug traits like crystal kind, uniformity of drug and release of drug), stability(that shows the degradation product), and effect of manufacturing parameters to verify that the production of drug product is steady.

Analyst before the development of new technologies, do not forget below mention criteria:

- Is this technique possesses the needful sensitivity?
- Is this method sufficiently selective for direct use without interference by means of the opposite element within the sample?
- Is the accuracy and precision doable with this technique?
- Are the reagents and equipment required on this method available or obtained at a reasonable price?
- Is the time requires to perform this technique applicable [3]?
- Steps for developing a method

Various steps are involved in the development of an analytical method are as follows:

- Characterization of analyte and standard

•All the known necessary data concerning the analyte and its structure that is to mention the physical and chemical properties such as solubility, optical isomerism, etc., are collected.

•The standard analyte is equal to 100% purity is acquired. Necessary arrangement is to be created for the proper storage (refrigerator, desiccators, and freezer).

•In the sample matrix, when multiple parts are to be measured the amount of elements is observed duly presenting the information and the accessibility of standard are calculated.

•Techniques like spectroscopy (UV-Visible, FTIR, atomic absorption spectroscopy, etc.), high-performance liquid chromate-graphy and gas chromatography so on and, are however about once coordinated with the stability of samples [2].

- Requirement of the technique: Requirement of analytical methodology is essential to build up the analytical fig. of advantage like linearity, selectivity, specificity, range, accuracy, precision, LOD, LOQ etc. shall be outlined [2].
- Literature survey and prior methods: All the data of literature related to the drug are reviewed for its physical and chemical properties, manufacturing, solubility and applicable analytical ways with reference to relevant books, journals, united states pharmacopeia/national formulary(USP/NF), association of official agricultural chemists (AOAC) and american society for testing and materials (ASTM) publications and it is extremely convenient to look Chemical Abstracts Service automatic computerized literature [2].

1.2 Validation

Validation is an idea that has developed in the U. S. in 1978. The idea of validation has extended during that time to grasp an extensive variety of activities from analytical approaches utilized for the quality control of medication to computerized systems for clinical trials, marking or process control, validation is established on, however not endorsed by regulatory specifications and is best seen as a critical and necessary part of current good manufacturing practice (cGMP).

The phrase validation basically implies for evaluation of validity or activity of demonstrating viability. Validation is a workforce effort where it entails humans from various departments of the plant. Validation is needed for any new or amended technique to confirm that it is capable of giving consistent and reliable results, once utilized by different operators using similar instrumentation within the same or completely different laboratories [8]. Validation is an essential component of quality assurance; it includes the efficient investigation of systems, facilities, and procedures aimed toward deciding if they execute their planned capacities sufficiently and reliably as determined.

Validation should in this way be considered in the accompanying circumstances:

- Completely new procedure.
- Latest equipment.
- Procedure and equipment which have been adjusted to suit altered needs and,
- Procedure where the finished result test is a poor and undependable marker of product quality [4].

1.2.2 Types of validation

Validation is classified into following types

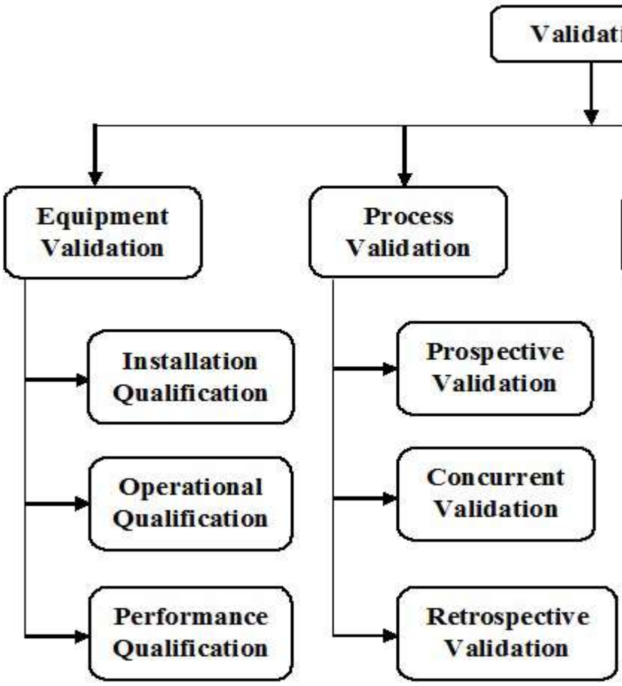

Figure 2: Validation types [9]

1.2.2.1 Equipment validation

- The key concept of validation is to give a high degree of reported confirmation that the equipment and the procedure conform to the written guidelines. The degree (or intensity) is dictated by the complexity of the device or system. The validation should give the essential data and test methods required to give that the device and technique meet determined prerequisites. Equipment Validation includes the following:
- Installation qualification (IQ): IQ guarantees all crucial processing, packaging system, and ancillary items are in compliance with the installation. It checks that the equipment has been established or installed as per the manufacturer’s suggestion in a systematic way and positioned in surrounding appropriate for its meant purpose [10].

1.2.2.2 Process validation

Prospective validation: It is described as the well-known reported program that a device does what it indicated to do based on pre-planned protocols. This validation is normally performed previously for distribution both of a newer item or item made under a revised production process [12]. In this validation, the protocol is accomplished before the procedure is placed into industrial use [8].

Prospective validation ought to incorporate, however, not be limited to the subsequent:

- Short depiction of the procedure.
- Summary of the important processing steps to be evaluated.
- Equipment/facilities list is to be utilized (involving calculation, observing/recording equipment) collectively with its calibration status.
- Finished dosage forms for discharge.
- List of analytical techniques, as suitable.

- Proposed in-process controls with specification criteria.
- Additional testing to be completed, with specification limits and analytical approval, as suitable.
- Sampling design.
- Techniques for recording and assessing outcomes.
- Functions and obligations.
- Proposed timetable [13].

Concurrent validation: It is same as prospective validation with the exception of the working firm, will offer the product at the time of qualification runs, to the society at its market cost, and furthermore like retrospective validation. This type of validation includes in-process observing of vital processing steps and product checking out. This helps to produce and reported proof to demonstrate that the manufacturing technique is in a condition of control [12].

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- In remarkable conditions, it might be acceptable not to finish the validation program before routine manufacturing begins.
- The choice to complete simultaneous approval must be supported, archived and accepted by authorized personnel.
- Documentation prerequisites for simultaneous validation are similar as designated for prospective validation [13].

Retrospective validation: It is characterized by the established reported confirmation that a system does what it implies to do on the audit and investigation of historical data. This is accomplished by the survey of the ancient manufacturing testing information to demonstrate that the procedure has always remained in control. This kind of approval of a procedure for an item already in distribution. Retrospective validation is adequate for well-established procedures and will be wrong where there have been current modifications within the composition of the product, working methods or device [12].

Few basic components of retrospective validation are:

- Batches are produced for a definite duration (last 10 successive batches). The number of lots discharged every year.
- Batch size/strength/producer/year/period.
- Master manufacturing/packaging files.
- Current particulars for active ingredients/finished materials.
- List of process deviations, corrective actions, and modification to production archives.
- Data for stability study for a few batches [13].

Revalidation: Revalidation gives the proof that modifications in the procedure, as well as the procedure condition that are presented don't unfavorably influence process attributes and product quality. Organizations, facilities, equipment and methods which include cleaning, ought to be periodically assessed to affirm that they stay valid. Where no remarkable modifications have been made to the approved status, a review with proof that facilities, organizations, equipment and procedures address the recommended necessities satisfies the need for revalidation [13].

Revalidation becomes vital in specific circumstances. Few of the modifications that require validation are mentioned below:

- Modifications in crude materials.
- Modifications in the equipment.
- Modifications in the source of active crude material producer.
- Alteration of packing material.
- Modification of the procedure.
- Modifications inside the plant/facility.
- A selection is no longer to carry out revalidation studies have to be completely justified and reported [13].

1.4 Validation parameters

The main aim of method validation is to produce proof that the method will what it is supposed to do, accurately, reliable and consistent [9]. The validation parameters as per ICH guidelines are described below:

Accuracy: Accuracy is expressed as the nearness of agreement between the values found and values that are already available. It can also be defined as the closeness between the true value and the observed value. It is sometimes called as trueness, and it could be determined by using at least 9 determinations over a minimum of 3 concentration over the specified range [19]. Accuracy of prochlorperazine maleate (PRO) and betahistine hydrochloride (BET) was studied by the standard addition method at three different levels (50%, 100%, and 120%). A known amount of drug was added to the pre-analyzed sample and percentage recovery calculated. When this method was used for accuracy, the recovery was found to be 99.38% for betahistine hydrochloride and 99.11% for prochlorperazine maleate [20].

For the concurrent determination of nitazoxanide and ofloxacin accuracy was studied by the standard addition method at five different levels (50%, 75%, 100%, 125%, and 150%). The results indicate that the recoveries were observed to be in the range of 80% to 120%, therefore, the method is accurate [21].

Accuracy of paracetamol was studied by preparing standard solution of different concentrations (10, 35, 55 µg/ml) and injected to check the % recovery. The percent recovery of the drug was found in the range of 98.8 to 102.0% respectively for all concentrations [22].

Precision: The exactness of an analytical procedure expresses the nearness of agreement (degree of scatter) between a group of measurements obtained from different sampling of a uniform sample underneath the prescribed conditions [23]. Precision may be taken into consideration at 3 levels:

Repeatability: It expresses the exactness below a similar operating condition over a brief interval of time and also referred as intra-assay precision. A minimum of six replicates test preparation of a similar or consistent sample ready at the 100% check [24].

Intermediate precision: It expresses the exactness under inside research laboratories, in distinct days, through distinct analyst, on distinct instruments/equipment. Two different analysts each preparing six sample solutions, as per specified method [25].

Reproducibility: It refers to the precision between different analytical labs. Every research facility set up an aggregate of six sample solutions, according to the analytical technique [24].

The precision of prochlorperazine maleate (PRO) and betahistine hydrochloride (BET) method was determined by interday and intraday variation (% RSD)

Specificity: For every stage of development, the analytical technique should demonstrate specificity. The technique was should have the power to unequivocally assess the analyte of interest whereas within the presence of all expected parts, which can encompass degradants, excipients/sample matrix, and sample blank peaks [26].

Limit of detection (LOD): Lowest quantity of an analyte which may be detected by the chromatographical separation however it is not necessary that this quantity will quantify as a precise value. A blank resolution is injected and peak to peak quantitative noise relation we have to calculate from blank chromatograms. Then, calculate the concentration at the signal to quantitative noise relation is concerning 3:1.

Linearity: Linearity may be characterized as the capacity of an analytical technique to produce outcomes which are directly related to the concentration of an analyte in the [30].

Range: It can be characterized as the interval amongst upper and lower quantities of analyte in the sample. Minimum of the specified range to be 80% to 120% of the test sample for the assay test [31].

Ruggedness: Ruggedness is the degree or measure of reproducibility under different situations such as in different laboratories, different analyst, different machines, environmental conditions, operators etc. [32]. In the simultaneous estimation of nitazoxanide and ofloxacin, ruggedness was performed by different analyst and in different laboratories in different days to checks for any variation in the chromatography. The % RSD for area and retention time was calculated for determination [21].

Robustness: It is characterized by the level of ability of an analytical technique, to stay similar by minute purposely change in the technique parameter. The different technique parameters which can be modified in high-performance liquid chromatography are pH, drift rate, the temperature of the column and mobile phase composition [33].

System suitability parameters: System suitability test is used to check the sensitivity, resolution, and reproducibility of the chromatographic system are well for the analysis to be done. The factors mainly used in system suitability are tailing factor, a number of the theoretical plate, retention time, resolution, etc. [34].

Tailing factor (T): It is defined as the distance between the front edge of the peak to the back edge of the peak divided by twice of the front edge of the peak.

$T = (X+Y)/2X$

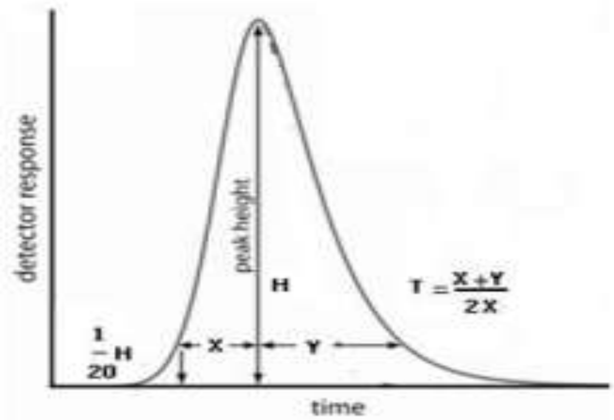

Figure 3: Tailing factor [35]

Where X = Front edge of the peak and,
Y = Back edge of the peak [35].

Capacity factor (K)): It can be expressed as how many times the analyte is retained with respect town retained compound. It is denoted by the symbol k.

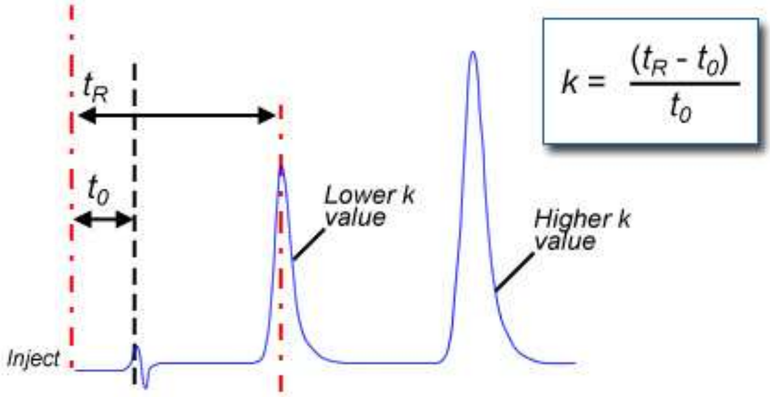

Figure 4: Capacity factor [36]

It can be calculated as:

$K = (t_R - t_0)/t_0$

Where t_R is the retention time of the peak and t_0 is the column dead time [27].

It is mainly utilized to examine the efficiency of the column. It can be expressed as:

$N = 16(t_R/W)^2$

Where t_R is the retention time, and W is the width at the base of peak [35].

Retention time (t_R): It is the time of elution of the peak after injection of the compound. The retention time of compounds will vary depending upon:

- Temperature of the column,
- Composition of solvents,
- Nature of stationary used and,
- Pressure used [37].

Resolution (R): It is the measure of separation power of the complete chromatographic system. Resolution can be defined as the ratio of the distance between two peak maxima to the mean value of peak width from its baseline.

$R = 2[(t_R)_{A-}(t_R)_B]/W_{A+}W_B$

Where, t_{R1} and t_{R2} are retention time of second and first compounds, respectively [35].

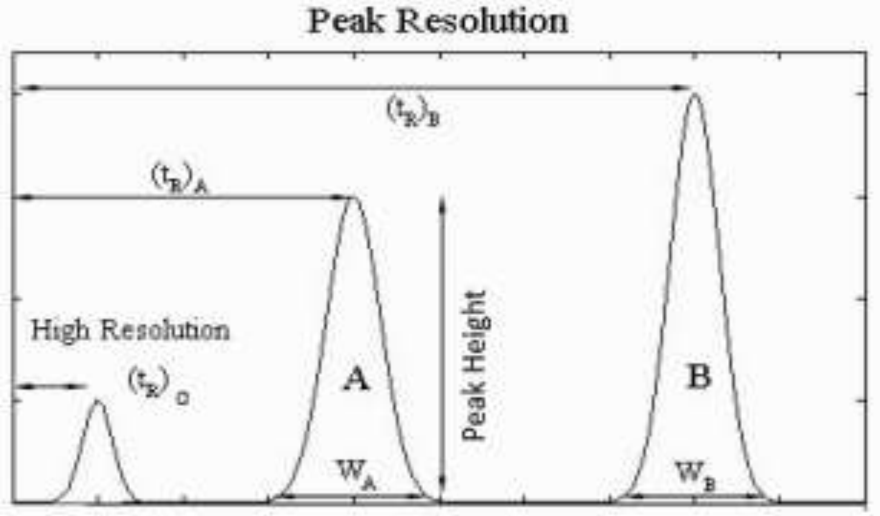

Figure 5: Resolution [35]

In the simultaneous estimation of nitazoxanide and ofloxacin, system suitability parameters was checked by injecting five injections of standard mixed solutions and two injections of the sample. The % RSD of both the drugs is less than 0.2% [21].

Review of literature

- Kotecha et al (2018) developed and validated Q-ABSORBANCE RATIO UV-spectrophotometric method for simultaneous estimation of metformin and canagliflozin in bulk and combined dosage form. They developed A rapid, simple, accurate and precise UV spectrophotometric Q-absorption ratio method was as per the ICH-Q2 guidelines for the simultaneous estimation of Metformin and Canagliflozin. The method involved Q-absorption ratio analysis using two wavelengths obtained by the overlay spectrum of the Metformin and Canagliflozin, with one being the maximum absorbance wavelength of Canagliflozin (220 nm, 2) and the other being the iso-absorptive point of both drugs (250 nm, 1). The method was validated as per ICH guidelines. Linearity and range were determined by analyzing six independent concentration levels of calibration curve in the range of 5-17.5 μg/mL for Metformin and Canagliflozin respectively (n=3). The value of correlation coefficient was > 0.99 for each of Metformin and Canagliflozin at 220nm and 250 nm. Accuracy of the method was confirmed by recovery study from marketed formulation at three levels – 80,100 and 120% of standard addition; the accuracy ranged between 99.63 and 101.14%. Intra-day and inter-day precision of Metformin and Canagliflozin was determined for three concentrations 5, 10 and 17.5 μg/mL at 220 nm, 240 nm and 250 nm; and % CV was <1.0%. The proposed UV spectrophotometric Q-absorption ratio method is rapid, simple, precise, reproducible and economical that can be successfully employed for the industrial analysis of the combination of Metformin and Canagliflozin [74].
- Sujana et al (2011) developed and validated UV Spectroscopic method of simultaneous determination of metformin and pioglitazone hydrochloride. Difference spectrum obtained, by keeping Pioglitazone and Metformin separately in 0.1M NaOH in sample cell and 0.1M HCl as blank, showed characteristic peaks(λmax) at 228.1nm (PIO) and 228.2nm (MET) and the characteristics peaks for pharmaceutical formulations were also found. This was depicted by plotting the graphs between wavelength and absorbance. Difference of absorbance between these two maxima was calculated to find out the amplitude, which was plotted against concentration. The optical characteristics for this method are precise and accurate. The proposed method can be applied to pharmaceutical formulations and the common excepients present in the formulation did not interfere with proposed method. The results indicate that the method is simple, sensitive and can be used for routine estimation of Pioglitazone and Metformin in pharmaceutical dosage form [87].

3.2 Literature of pravastatin sodium

- El-Olemy et al (2017) developed and validated UV Spectroscopic method of simultaneous determination of Pravastatin Sodium and Pioglitazone Hydrochloride in Pharmaceutical Preparations. The first method is the first derivative, where the peak amplitudes of first derivative of absorption spectra were measured at 249.7 and 277 nm for pravastatin sodium and pioglitazone hydrochloride respectively. The second method is the first derivative of the ratio spectra, where the peak amplitudes were measured at 249.6 and 276.6 nm for pravastatin sodium and pioglitazone hydrochloride respectively. The proposed methods were validated according to International Conference on Harmonization (ICH) guidelines and successfully applied for simultaneous determination of both drugs in their combined dosage form. The proposed methods are simple, rapid, economic, accurate and precise to simultaneously determine pravastatin and pioglitazone in pure form and in pharmaceutical dosage form without previous separation steps [88].

- Stolarczyk et al (2017) developed Spectrophotometric method for simultaneous determination of valsartan and substances from the group of statins in binary mixtures. Applicability of derivative spectrophotometry for the determination of valsartan in the presence of a substance from the group of statins was checked. The obtained results indicate that the proposed method may be effective by using appropriate derivatives: for valsartan and fluvastatin– D1, D2 and D3, for valsartan and pravastatin – D1 and D3, for valsartan and atorvastatin – D2 and D3. The method was characterized by high sensitivity and accuracy. Linearity was maintained in the following ranges: 9.28–32.48 mg mL–1 for valsartan, 8.16–28.56 mg mL–1 f or fluvastatin, 14.40–39.90 mg mL–1 for atorvastatin and 9.60–48.00 mg mL–1 for pravastatin. Determination coefficients were in the range of 0.989–0.999 depending on the analyte and the order of derivative. The precision of the method was high with RSD from 0.1 to 2.5 % and recovery of individual components was within the range of 100 ± 5 %. The developed method was successfully applied to the determination of valsartan combined with fluvastatin, atorvastatin and pravastatin in laboratory prepared mixtures and in pharmaceutical preparations [89].
- Bodiwala et al (2014) developed and validated pH independent spectrophotometric method has been developed for the determination of pravastatin sodium in pharmaceutical formulations. The method is based on the measurement of absorbance at isosbestic point. Isosbestic point for pravastatin sodium was observed at 249 nm and absorbances were measured at same wavelength. The method is found to be linear in the range of 2.5–30 µg/mL for pravastatin sodium with R2= 0.9996 (n=5). The proposed method is simple, rapid and gives accurate and precise results. Market formulations of pravastatin sodium were analyzed with the proposed method. Results obtained are in good agreement with the labeled amount of pravastatin sodium (100.62 ± 0.63, n=3) in tablet dosage forms**.** The proposed method can be satisfactorily applied for estimation of Pravastatin sodium in pharmaceutical dosage form. The method can also be applied for estimation of Pravastatin sodium in aqueous medium irrespective of pH of solution [90].
- Ashour et al (2011) developed A simple and sensitive kinetic spectrophotometric method for the quantitative analysis of pravastatin sodium (PVS) in pure and pharmaceutical formulations. The method is based on the formation of colored product between PVS and 4-chloro-7-nitrobenzo-2-oxa-1,3-diazole (NBD-Cl) in acetone medium at 55± 2°C. The reaction is followed spectrophotometrically by measuring the increase in absorbance at 462 nm as a function of time. The initial rate and fixed time methods were adopted for constructing the calibration curves. The linearity ranges were found to be 15.0– 50.0 and 10.0–70.0 µg/ml for initial rate and fixed time methods, respectively. The limits of detection for initial rate and fixed time methods are 0.029 and 0.086 µg/ml, respectively. Both methods have been applied successfully for the estimation of PVS in commercial dosage forms with no interference from the excipients. The results are compared with the HPLC pharmacopoeial method [91].

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