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An Overview on Analytical Method Development & Validation of Drug: Amitriptyline HCL Using HPLC

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ABSTRACT: -

The current article consists of a review and literature about the use of the drug Amitriptyline Hcl as an antipsychotic, antidepressant drug along with its analytical features. Here we have also discussed about the analytical methods that can be carried out such as spectroscopy, chromatography etc. Analytical techniques can be roughly divided between classical and instrumental techniques. Volumetry (titrimetric), gravimetry, gasometer, and other antiquated techniques are examples of the former classical techniques. Spectroscopic techniques (UV-Visible, FS, AS, IR, NMR, etc.). Electrophoreticmethods, Chromatographic methods (CC, TLC, HPTLC, HPLC, GC, etc.), and other instrumental methods. An overview of the analytical techniques used to analyse the drug amitriptyline is provided in this publication. This article will help to gain deep knowledge and previous work done Amitriptyline HCL.The article also provide information about the forced degradation studies and procedure to perform degradation studies according to ICH guidelines.

Keywords: -Amitriptyline Hcl, Analytical method development,Analyticalvalidation,Hplc, Degradation studies

INTRODUCTION: -

Antidepressant medications and related studies will be examined in this study. We shall go over the reported analysis techniques for the medications in this post. In order to do further research Three-ring chemical compounds known as tricyclic antidepressants (TCAs) have been used extensively in clinical practise to treat a variety of depressive disorders, including phobias, insomnia, chronic pain syndromes, panic disorder, eating disorders (such as bulimia nervosa), premenstrual dysphoric disorder, and anxiety disorders[1]. These illnesses have a negative impact on the patients' social and economic well-being, which can ultimately result in suicidal behaviour. Antidepressants are frequently administered in various combinations, increasing the likelihood of drug-drug interactions while relying heavily on trial-and-error dosing. Pharmacologically and structurally, tricyclic antidepressants are all quite similar. Three significant neurotransmitters—serotonin, norepinephrine, and dopamine—that are normally taken up by brain cells in the central nervous system are inhibited by these medications under normal circumstances. Chemically, amitriptyline hydrochloride is known as 3-(10, 11-dihydro-5H-dibenzo [ad] cycloheptene-5-ylidine)-N,N-dimethyl-1-propanamine hydrochloride. It is a tricyclic antidepressant. It is a crystalline substance that is white, colourless, and freely soluble in water. Many psychiatric problems are treated with it. The typical daily dosage ranges from 50 to 200 mg. Amitriptyline hydrochloride have some positive effects, but when taken in excess, it has a number of negative side effects and can include cardiac depression, hyperreflexia, convulsions, and unconsciousness [1,2].

1.0 ANALYTICAL METHOD DEVELOPMENT

INTRODUCTION

Every year, there are more medications made available on the market. These medications could be brand-new substances or ones that have had some structural changes made to them. A drug's introduction to the market and the date of its inclusion in pharmacopoeias frequently occur at different times [3]. This occurs as a result of potential ambiguities in the continued and expanded use of these medications, reports of new toxicities (leading in their removal from the market), the emergence of patient resistance, and the launch of superior medications by rival companies. Under these circumstances, the pharmacopoeias may not provide standards and analytical techniques for these medications. Thus, the creation of more modern analytical techniques for such medications is required [4]. The development of analytical methods must follow the guidelines outlined in the International Conference on Harmonization (ICH) recommendations (Q2A and Q2B) and should be done in accordance with good manufacturing practise (GMP) and good laboratory practise (GLP) conditions. [4,5] The ongoing

process of method development moves on in lockstep with the development of the therapeutic product. The goal and purpose of the method should reflect the phase of drug development. The strategies may concentrate on API behaviour throughout the early stages of drug development. Preclinical safety assessments, pre-formulation investigations, and stability tests on prototype products must to be supported by them. The analytical methodologies are improved and broadened as drug research advances, depending on greater understanding of the API and therapeutic product. The procedures must adhere to the necessary regulatory requirements while being reliable and simple. Prior to conducting formal validation experiments, scouting experiments are usually carried out throughout the technique development process to determine the performance bounds of the approach [6–9]. This could involve forced degradation studies, which are essential to the creation of a stability-indicating approach. Acid, base, peroxide, heat, and light are commonly the degrading agents for API. As a result, it is possible to assess the method's ability to identify and quantify degradation products while learning more about the primary mechanisms underlying degradation. Once a stability-indicating method has been established, the formed medicinal product can next be exposed to heat and light to assess any potential API degradation in the presence of formulation excipients. [6]

1.1 ANALYTICAL METHOD VALIDATION

In Analytical Method Validation, an Analytical Process is the most crucial element. The analytical process specifies the qualities of the drug substance or product and provides acceptance standards for those qualities. There are two different kinds of analytical procedures: the first are the specifications and common test techniques found in pharmacopoeias or pharmacopeial methods, and the second are non-pharmacopeial methods or methods created internally and accepted by the national regulatory authority.[5]

Analytical method validation is primarily carried out for the following test procedures:

1. Identification tests;
2. Quantitative tests for impurities content;
3. Limit tests for the control of impurities;
4. Quantitative tests of the active moiety in samples of the drug substance or drug product or other chosen component(s) in the drug product.

Analytical method validation characteristics which should be considered during performing of method validation;

1. Accuracy.
2. Precision.
3. Specificity.
4. Detection Limit.
5. Quantification Limit.
6. Linearity.
7. Range.
8. Robustness.

1 ACCURACY: -

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. This is sometimes termed trueness. It is normally established on samples of the material to be examined that have been prepared for quantitative accuracy. Accuracy should be established across the specified range of the analytical procedure.

This test is mainly to check the recovery of API with Placebo. analyst have to prepare sample solution in triplicate of API with Placebo at different minimum 3 concentrations (e.g., 80%, 100% & 120%) it will give nine results. Acceptance criteria of this test should %recovery at each concentration ±5 % and % RSD should be no more than 5.0. Accuracy should be reported as percent recovery by the assay of the known added amount of analyte in the sample or as the difference between the mean and the accepted true value together with the confidence intervals.

2 PRECISION: -

Precision is the degree of closeness of agreement among individual test results when the method is applied to multiple sampling of a homogeneous sample.

Precision is repeatability Six replicate of concentration of Intraday Precision and Interday Precision Variations of results within the same day (intra-day), variation of results between days (inter- day) were analyzed. Intra-day precision was determined by analysing both standard solutions for three times in the same day. Interday precision was determined by analysing the drugs daily for three days. %RSD was calculated. [5,8]

3 SPECIFICITY:-

While validating identification tests, identifying contaminants, and performing assays, specificity should be investigated. The methods used to prove specificity will vary depending on the analytical procedure's intended goal. It's not always possible to prove that an analytical method is unique to a certain analyte (complete discrimination). In this instance, it is advised to combine two or more analytical techniques to reach the required level of discrimination.

4 LOD and LOQ: -

The limit of detection (LOD) and limit of quantification (LOQ) were calculated experimentally. Calibration curve was repeated for five times and standard deviation (SD) of the intercepts was calculated. The LOD and LOQ of the drug were derived by calculating the signal-to-noise (i.e., 3.3 for LOD and 10 for LOQ) ratio using following equations designated by International Council for Harmonization (ICH) guideline:

LOD = 3.3 X σ/S

and LOQ = 10 X σ/S

Where, σ = standard deviation of the response S = Slope of the calibration curve [(9)]

5 LINEARITY & RANGE

A linear relationship should be evaluated across the range of the analytical procedure. It may be demonstrated directly on the drug substance (by dilution of a standard stock solution) and /or separate weighing's of synthetic mixtures of the drug product components, using the proposed procedure. The latter aspect can be studied during the investigation of the range

Linearity is the ability of the method to produce results that is directly proportional to the concentration of the analyte in samples with given range. From the linearity studies calibration curve was plotted and concentrations were subjected to least square regression analysis to calculate regression equation. The regression coefficient should be 0.999 and show good linearity of the drug. [(9)]

6 ROBUSTNESS:

The robustness is evaluated by the analysis of drugs under different experimental conditions such as making small changes in flow rate (±0.2 mL/min), λ max (±5), column temperature (±5), mobile phase composition (±5%), and pH of the buffer solution.[8,9]

1.2 NECESSITY OF ANALYTICAL METHOD DEVELOPMENT AND VALIDATION

- Method Development is a series of steps that defines and optimises analytical test parameters to determine the capabilities of the test method.
- It provides a high degree of assurance that the test procedure will reach or exceed the required standard.
- Before use, the developed method must have completed the appropriate validation.
- It is important to conduct regular reviews as method development proceeds.
- Using method recommendations to standard test techniques for testing new products or materials might improve performance testing.

The testing parameters are found during the method development phase to ensure the data's applicability and reliability. [10,31]

2.0 FORCED DEGRADATION STUDIES

Pharmaceutical molecules' chemical stability is a major problem because it has an impact on the drug's safety and effectiveness. To understand how the quality of a drug substance and drug product changes over time under the effect of diverse environmental conditions, the FDA and ICH guidelines specify the demand for stability testing data [11]. In order to provide adequate formulation, packaging, storage conditions, and shelf life, regulatory documentation must have knowledge of the stability of the molecules. Forced degradation is a procedure that includes breaking down drug products and drug substances under less favourable conditions than those used in accelerated degradation. As a result, degradation products are created that may be examined to find out how stable a molecule is. The ICH guideline states that stress testing is intended to identify the likely degradation products which further helps in determination of the intrinsic stability of the molecule and establishing degradation pathways, and to validate the used stability indicating procedures [13] In the pharmaceutical industry, forced degradation studies give a method for analysing the stability of pharmaceutical samples. The chemical stability of the molecule has an impact on the safety and effectiveness of drug products. Determining a molecule's stability facilitates the selection of an appropriate formulation and packaging as well as the selection of suitable storage conditions and shelf life, which are all necessary for regulatory validation. [13,30] Forced degradation is a procedure where drug products and drug compounds are degraded under conditions that are severe than accelerated conditions. This approach generates degradation products that may be analysed to find out how stable a molecule is. The necessity for the development of a stability-indicating assay method (SIAM) has

become more clearly specified with the advent of The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)guidelines. [13,14]

The International Conference on Harmonization (ICH) standards clearly define forced degradation of novel medicinal products and make it necessary to plan forced degradation studies. These investigations provide the knowledge to aid in the identification of probable degradation agents. Additionally, it shows whether pharmaceutically useful compounds decompose. Studies on forced degradation can be used to determine the intrinsic stability of medicinal molecules. Forced degradation studies can also be used to assess differences between drug-related degradation and excipient interferences as well as possibly polymorphic or enantiomeric compounds. The forced degradation studies under a variety of conditions, such as pH, light, oxidation, dry heat, acidic, basic, hydrolysis, etc., are required by ICH recommendations (as shown in figure 1) [15,29]

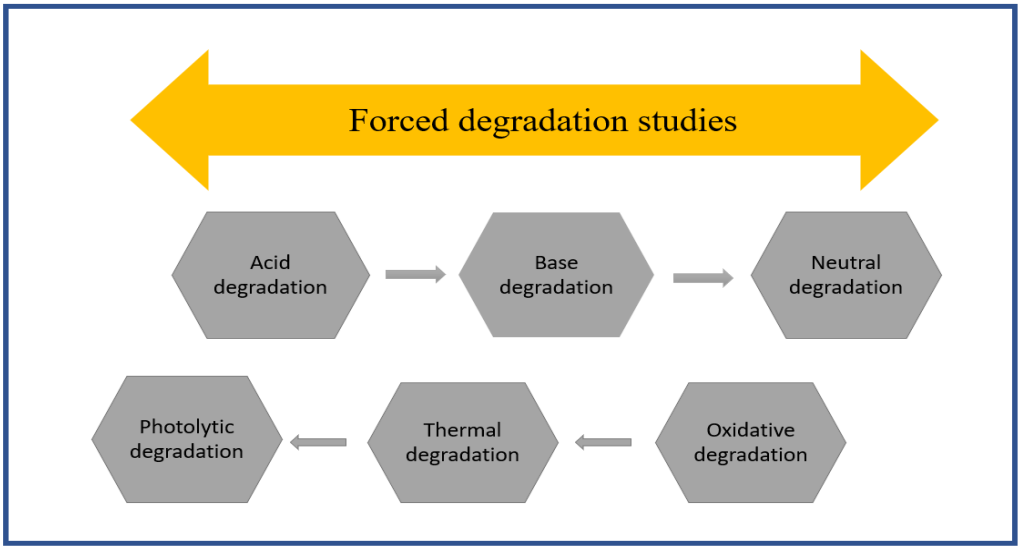

Fig 1 {Degradation Studies}

1. ACID/BASE DEGRADATION

One of the most typical chemical processes for deterioration across a broad pH range is hydrolysis. Drugs react with water in a solvolytic process called hydrolysis to produce breakdown products with various chemical makes-ups. Acid or base stress testing entails exposing a pharmacological material to acidic or basic conditions that produce primary degradants in a desired range in order to compel its forced degradation. The type and concentration of acid or base that are chosen will depend on how stable the pharmacological ingredient is. As acceptable reagents for hydrolysis, sodium hydroxide or potassium hydroxide (0.1-1 M) are proposed for base hydrolysis and hydrolytic acid or sulfuric acids (0.1-1 M) for acid hydrolysis. When a compound is difficult to dissolve in water, co-solvents can be added to make it easier to dissolve it in HCL or NaOH. The structure of the drug substance is used to guide the choice of co-solvent. Normal stress testing trials begin at room temperature, and if no degradation occurs, high temperature (50–70ºC) is next applied. A maximum of seven days should be allowed for stress testing. To stop further degradation, the degraded sample is subsequently neutralised with the appropriate acid, base, or buffer.[16]

2. OXIDATIVE DEGRADATION

In forced degradation investigations, hydrogen peroxide is frequently used to oxidise the drug compounds, although other oxidising agents, such as metal ions, oxygen, and radical initiators (such as azobisisobutyro -nitrile, AIBN), can also be employed. The drug substance determines the type of oxidising agent to use, as well as its concentration and environmental factors. It has been suggested that exposing the solutions to 0.1–3% hydrogen peroxide for seven days at neutral pH and room temperature, or up to a maximum 20% degradation, may produce significant degradation products. An electron transfer mechanism is used in the oxidative breakdown of pharmacological material to produce reactive cations and anion. Electron transfer oxidative may transform amines, sulphides, and phenols into N-oxides, hydroxylamine, sulfones, and sulfoxide. The oxidation of functional groups containing labile hydrogen, such as those with benzylic, allylic, tertiary, or -positions with respect to hydrogen atoms, can result in the formation of hydroperoxides, hydroxide, or ketone.[16]

3.PHOTOLYTIC DEGRADATION

To enable direct comparisons between the drug substance and drug product, samples should be exposed to light providing an overall illumination of not less than 1.2 million lux hours and an integrated near ultraviolet energy of not less than 200-watt hours/square metre with a spectral distribution of 320–400 nm, as per the ICH Q1B guideline for photo degradation. Samples could be treated simultaneously with a tested chemical when circumstances have been monitored

using calibrated radiometers/lux metres, an actinometric system should be used to verify the desired light exposure is obtained. The pharmacological compounds are exposed to UV or fluorescent light during photolytic degradation investigations. According to the ICH Q1B guidelines, the drug compounds or drug products (solid or liquid) are exposed to the light source in this study. For investigations on degradation, a typical radiation range is between 300 and 800 nm. In a photolytic situation, oxidation through a free radical mechanism or a non-oxidation process causes the degradation. Isomerization, dimerization, and other processes are included in non-oxidative degradation. On the other hand, the oxidative photolytic reaction uses a singlet/triplet oxygen state-based mechanism.[16]

4. THERMAL DEGRADATION

Thermal degradation (such as dry heat and wet heat) ought to be performed under more difficult conditions than suggested ICH. Accelerated testing circumstances for Q1A. Solid-state drug substance and drug product sample the liquid medicine should be exposed to both dry and wet heat. Products ought to be heated dry. Research may be conducted for a shorter time at a greater temperature. Impact of temperature on a material's thermal degradation. The Arrhenius equation is used to study substance.

K = Ae-Ea./RT

where K is specific reaction rate,

A is frequency factor,

Ea. is energy of activation,

r is gas constant (1.987 Cal/deg/ mole)

T is absolute temperature.

Thermal degradation study is carried out at 40-80^{0}C [17]

2.1 OBJECTIVE OF FORCED DEGRADATION STUDIES

The following goals are pursued through forced degradation studies:

1. To identify the processes by which drug compounds and drug products degrade.

2. To distinguish in a formulation between degradation products produced from non-drug items and those connected to drug products.

3. To clarify the degradation products' structure.

4. To ascertain a pharmacological substance's inherent stability in formulation.

5. To identify how the drug material and drug product degrade, for as by hydrolysis, oxidation, thermolysis, or photolysis.

6. To demonstrate the stability of a proposed method.

7. To comprehend the chemistry of medication compounds.

8. To produce formulations that are more stable.

2.2 NEED FOR FORCED DEGRADATION OF DRUGS

Studies on forced degradation of drug molecules are very important in the following aspects.

1. To create techniques for assessing stability.

2. To identify the mechanisms for deterioration.

3. To assess the drug's intrinsic stability in dose formulations.

4. To research molecules' chemical makeup.

5. To create formulas that are stable.

6. To identify the breakdown products' structural makeup.

7. To address stability-related issues.

8. To create an ICH-compliant degradation profile [18,19]

3.0 AMITRIPTYLINE HCL

Tricyclic antidepressant amitriptyline also functions as an analgesic. It is unknown if its analgesic benefits are related to its mood-altering activity, a specific pharmacological action, or a combination of both (or neither). Clinical studies show that oral amitriptyline produces at least a fair or moderate response in up to two-thirds of patients with painful diabetic neuropathy and post-herpetic neuralgia, neurogenic pain disorders that are frequently refractory to narcotic analgesics. Amitriptyline has been proven effective in a variety of patient populations with chronic, non-cancerous pain. Amitriptyline may also be used in fibromyalgia patients or as an adjuvant for uncontrolled cancer pain, though the evidence for these uses is weaker. Even at the low dosages used for pain management, adverse effects related to the antimuscarinic activity of amitriptyline (mainly dry mouth and sedation) are frequently reported. These effects might be minimised with low initial doses and proper dosage titration. The elderly may also experience issues with orthostatic hypotension and tachycardia, which are occasionally linked to tricyclic antidepressant medications.

In conclusion, amitriptyline can be an effective treatment for chronic pain disorders that affect the elderly, but only if it is taken carefully to limit side effects. Amitriptyline is an essential and efficient therapeutic choice for post-herpetic neuralgia and diabetic neuropathy, and it continues to be the antidepressant medication that has been the subject of the most research in both diseases. [20,26]

3.1 PHARMACOLOGICAL PROPERTIES

Tricyclic antidepressant drugs' analgesic effects have been explained by one of two theories: either their analgesic effects are a by-product of their antidepressant effects, or they have separate analgesic effects. Clinical evidence indicates that analgesia might be induced independently of these drugs, antidepressant effects, although the exact mechanism by which this is accomplished is uncertain.

Amitriptyline has been shown to have analgesic effects in several animal models following either single or multiple doses, however it is unknown if these models are applicable to human chronic pain conditions. In two experiments, amitriptyline induced dose-dependent analgesia to each of three distinct painful stimuli. Amitriptyline is quickly absorbed after oral administration, however due to a significant first-pass impact, it has a low oral bioavailability. Amitriptyline's pharmacokinetics exhibit high interpatient variability, just like those of other tricyclic antidepressants. The medication is highly protein bound and broadly disseminated throughout the body. In the liver, amitriptyline undergoes substantial metabolism; the main metabolite, nortriptyline, has pharmacological activity. Amitriptyline has a terminal elimination half-life of between 12.9 and 36.1 hours. Age has not been shown to have a definite impact on the pharmacokinetics of amitriptyline, albeit clearance may be affected [20]

3.3 THERAPEUTIC USE

After 3 to 6 weeks of treatment, oral amitriptyline reduced pain intensity by 21 to 46% compared to baseline in individuals with post-herpetic neuralgia that had been present for at least 3 months. A satisfactory or outstanding response to therapy was reported by 47 to 67% of patients. Amitriptyline considerably reduced pain when subjective assessment criteria were applied, compared to placebo or comparative drugs (lorazepam, zimeldine and maprotiline). After receiving amitriptyline for 6 to 8 weeks of treatment, up to 74% of patients with painful diabetic neuropathy reported experiencing good or moderate pain alleviation. Amitriptyline had a comparable impact to topical capsaicin (42%) or desipramine (28%), but it significantly reduced pain intensity (29 to 51%) more than the placebo (15%).[20]

3.4 DOSAGE AND ADMINISTRATION

Amitriptyline should be begun at a dosage of 10 to 25 mg per day and increased by 10 to 25 mg per week until the maximum advised or acceptable dosage is reached. Amitriptyline should be begun at a modest dosage (10 mg/day) and increased gradually in 10 mg increments to reduce the risk of adverse effects in the elderly. 75 mg per day is the recommended upper limit for the treatment of neurogenic pain. Amitriptyline should be used cautiously, like other tricyclic antidepressants, in individuals who have urinary retention, prostatic hypertrophy, glaucoma, constipation, poor liver function, or cardiovascular illness. It should be avoided in patients with severe liver illness, cardiac block, arrhythmias, or right after a myocardial infarction.[20]

4.0 DRUG PROFILE

ATTRIBUTES	**DESCRIPTION**
NAME	AMITRIPTYLINE HCL.
CATEGORY	ANTIDEPRESSANT, ANTINOCICEPTIVE
APPERANCE	WHITE POWDER

MOL. FORMULA	$C_{20}H_{24}ClN$
MOL. WEIGHT	313.864 g/mol
MELTING POINT	195-197ºC
SOLUBILITY	SOLUBLE IN WATER, ALCOHOL ETC

5.0 PREVIOUS WORK WHICH HAS BEEN DONE ON AMITRIPTYLINE HCL.

Sr. No	Title	Mobile Phase	Coloumn	Flow Rate	RETENTION TIME	UV
1	Analytical Method Development andValidation For Amitriptyline Hcl (Psychoactive Drug) Using HplcInstrument. (1)	Phosphate Buffer: Acetonitrile(55:45 % V/V) PH Of The Buffer 2.5 By Diluted Ortho Phosphoric Acid	Inertsil ODS 3V (150 Mm X 4.6 Mm, 5 µm	1 ml/Min 25°C	4 Minute	254 Nm.
2	Development And Validation Of Novel Rp-Hplc Method For Simultaneous Estimation Of Gabapentin And Amitriptyline Hydrochloride In Bulk And Pharmaceutical Dosage Forms (21)	0.05 M Potassium Dihydrogen And Acetonitrile (55:45) Orthophosphate Ph 2.1 Adjusted With Orthophosphoric Acid	Shim-Pack HPLC C18 Column (4.6 X 250 Mm, 5µm)	1 ml/Min 25°C	4.221 Min	221 Nm
3	RP-HPLC Determination ofAmitriptyline Hydrochloride In Tablet Formulations And Urine (23)	Acetonitrile And Water, (50 % V/V) Adjust Ph To 5 Using Phosphoric Acid	C18 Reversed-Phase Column (250 Mm X 4 Mm I.D. Of 250 Mm X 4 Mm	0.6 ml/Min 30^0C	7.3 min	254nm.
4	RP-HPLC Method Development And Validation For The Simultaneous Estimation Of Amitriptyline Hydrochloride And Pantoprazole Sodium In Bulk And Capsule Dosage Form (24)	Methanol And Phosphate Buffer (80:20v/V)	Cosmosil 18 (250 Mm × 4.6 Mm,5 mm) Column.	0.8 ml/Min.	3.21 minutes	244nm
5	Analytical Method Development and Validation of Amitriptyline Hydrochloride And Chlordiazepoxide In Tablet By Rp-Hplc(22)	Ortho Phosphoric Acid:Methanol In The Ratio Of 50:50 V/V (Adjust Ph -2 With Orthophosphoric Acid),	YMC Colimited C8 (250 X 4.6 Mm,5µ) Column	1.0ml/Min 40^0C	2.50 min	253 nm.
6	Development And Validation Of Stability Indicating Rp-Hplc Method For Simultaneous Estimation Of Gabapentin And Amitriptyline Hydrochloride In Its Pharmaceutical Dosage Form (8)	20 Mm Ammonium Acetate: Acetonitrile (65:35) %V/V. Ph 6.0	Water Symmetry250 X 4.6mm 5µ C18	1.0 Ml/Min 25°C	2.793± 0.01 min	(272 nm)
7	Development Of Validated Stability Indicating RP-UPLC Method For The Determination Of Amitriptyline	Potassium Dihydrogen Phosphate Buffer And Acetonitrile (35:65) Ph 3.0±0.05	Symmetryc18 (2.1mmx 100mmx 1.7 mm) Column	0.30ml/ Min	3.0min	239 nm.

	Hydrochloride In Bulk And Its Pharmaceutical Formulations (25)					

LITERATURE SURVEY

1. According To Sevak Dhaval Et Al,

His research manuscript describes simple yet sensitive, speedy, accurate and precise HPLC method for the analysis of Amitriptyline HCl in tablet form. The sample was analyzed by HPLC instrument using Inertsil ODS 3V (150 mm X 4.6 mm, 5 µm Make, GL science) column as stationary phase and Phosphate Buffer: Acetonitrile(55:45 % v/v) as a mobile phase (where PH of the buffer was adjusted to 2.5 by using diluted ortho phosphoric acid) at a flow rate of 1.0 ml/min. UV detector was used for the detection at 254 nm. The retention time for Amitriptyline HCl was found about 4 minutes. The linearity for the drug was obtained for the concentration of 45, 80, 100, 120 & 150µg/ml. This method would be successfully applied to pharmaceutical formulations because no significant interferences from tablet excipient were found. The method retained its accuracy and precision when certain variations in method parameters were applied

2. According To Sultana Shaikh Et Al,

In this work, good chromatographic separation was achieved isostatically using a shim-pack HPLC C18 column (4.6 x 250 mm, 5µm) and mobile phase consisting of 0.05 M potassium dihydrogen orthophosphate pH 2.1 adjusted with orthophosphoric acid and acetonitrile in the ratio (55:45), at flow rate 1 ml/min and column temperature (25 °C). The effluents obtained were monitored at 221 nm with the UV-visible detector. Results: The retention time of gabapentin and amitriptyline hydrochloride was found to be 1.959 min and 4.221 min respectively. The linearity of gabapentin was found in the range of 720-1680 ppm and that for amitriptyline hydrochloride was found to be 24-56 ppm. The correlation coefficient for gabapentin and amitriptyline hydrochloride were 0.999 and 0.9963 respectively. The high recovery values (98%-101%) indicate a satisfactory accuracy. The low percent relative standard deviation (% RSD) values in the precision study reveals that the method is precise. Hence the proposed method may find practical applications as a quality-control tool in the simultaneous analysis of the two drugs in combined dosage forms in quality-control laboratories.

3. According To Shaikh Siddiqui Et Al,

A simple, rapid, accurate and precise isocratic reversed phase high performance liquid chromatographic method has been developed and validated for Simultaneous Estimation of Pantoprazole Sodium (PNT) and Amitriptyline Hydrochloride in Bulk and Capsule Dosage Form. In RP-HPLC method, the analyte were resolved by using isocratic program, methanol and phosphate buffer (80:20v/v) was used as mobile phase, at a flow rate of 0.8 ml/min. on HPLC system containing UV-visible detector with Workstation software and cosmosil 18 (250 mm × 4.6 mm,5 µm) column. The detection was carried out at 244nm. The retention times were 3.21 minutes and 4.20 minutes for Amitriptyline Hydrochloride and Pantoprazole Sodium respectively. Calibration plots were linearity was found 0.9995 and 0.9997 for Amitriptyline Hydrochloride and Pantoprazole Sodium. The proposed method was successfully used for simultaneous estimation of Amitriptyline Hydrochloride and Pantoprazole Sodium in capsule dosage form. Validation studies revealed that the proposed method is specific, rapid, reliable and reproducible. The high % recovery and low % RSD confirms the suitability of the proposed method for routine quality control analysis of Amitriptyline Hydrochloride and Pantoprazole Sodium in bulk and capsule dosage forms.

4. According To Ashraf M. Ahmed Et Al,

His work proposed rapid and sensitive reverse phase HPLC method, was developed and validated for the determination of amitriptyline hydrochloride in tablet formulations and urine. The mobile phase used acetonitrile and water, (50 % v/v) adjust pH to 5 using phosphoric acid. The separation was achieved on C18 reversed-phase column (250 mm x 4 mm i.d.). The flow rate was 0.6 ml/min and UV detection at 254nm. The retention time for amitriptyline hydrochloride was 7.3 min. The calibration curve was linear in the range 0.5-3 µg/mL. The mean recovery for amitriptyline hydrochloride is 100.025 %. The assay was precise within day and between days. The method provided excellent sensitivity, recovery, accuracy, and reproducibility in therapeutic or toxic concentrations. And concluded that common excipients do not interfere.

5. According To Neeli Sujatha Et Al,

A simple, economic, selective, precise, and accurate Reverse Phase High Performance Liquid Chromatography method for analysis of Amitriptyline Hcl & Chlordiazepoxide in tablet dosage form was developed and validated according to ICH guidelines. The quantification of the drug was carried out by using YMC Colimited C8 (250 X 4.6 mm,5µ) column its equivalent in isocratic mode and maintain column at 400C, using mobile phase comprising of Ortho phosphoric Acid : Methanol in the ratio of 50:50 v/v (Adjust pH -2 with Orthophosphoric Acid), with a flow rate of 1.0mL/min and the detection wavelength was carried at 253 nm. The retention time for Amitriptyline Hcl & Chlordiazepoxide was found to be 2.502&5.176. The percent assay was found to be 101%&99%. Proposed method was validated for precision, accuracy, linearity & range, specificity and robustness according to ICH guidelines. The method was successfully applied to Amitriptyline Hydrochloride and Chlordiazepoxide combination Tablet dosage form.

CONCLUSION

In this article, the study was carried out on antidepressant, antipsychoticdrug: Amitriptyline Hcl. In addition, we have gone over the criteria used in developing and validating analytical methods. A brief description of an antidepressant, including its basic mode of action, side effects, and pharmacological classifications that fall within this category, is provided. We went into great length about the pharmacological profile of the antidepressant amitriptyline. The therapeutic applications of amitriptyline were discussed in great depth. All available amitriptyline studies and research were subjected to a detailed comparative analysis and literature assessment. The existing chromatographic techniques or methodologies for the qualitative and quantitative determination of amitriptyline in various pharmaceutical preparations were displayed in the literature. We may infer from the extensive historical research that was done that there hasn't been much analysis done on amitriptyline. Amitriptyline has not received enough attention from researchers or academics, and methods should be improved. In this way, we can take the decision to choose the drug amitriptyline, on the basis of the literature review conducted in this article. The drug's broad area of work in the field of analytical method development and validation, together with the force degradation studies that need to be done, could lead to a quick, accurate, and affordable way to determine how much amitriptyline is in a pharmaceutical dose form.

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