CHAPTER-8

Summary, Conclusion

&

Recommendations
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8.0 Summary, Conclusion and Recommendations

Drugs and pharmaceuticals are now days very important for mankind to make use as and when falls ill health. Due to drug interaction, the levels of the active drug may be too high for a longer time leads to number of side effects. Determination of drugs and its related impurities with help of suitable analytical techniques and development of sensitive, consistent, rapid and reproducible procedures acquire importance in this context. One of such effective analytical tool was HPLC/UPLC. These chromatographic techniques found most versatile and particularly employed in qualitative and quantitative analysis of drugs and pharmaceutical formulations. In view of its significance, these techniques were employed for selective drugs and formulations which are therapeutically used.

The first chapter related to introduction devoted for concise details about drugs, its importance in day to day life. Further, it was highlighted the importance of analytical techniques in the quantitative estimation of drugs and formulations along. Various kinds of quantification parameters were explained with their importance in analysis and for the development of stability indicating methods, contents of validation of analytical procedures

Second chapter is confined for literature survey. An extensive literature survey was made on the investigated compounds which are having significant role in the form of drugs and pharmaceutical formulations. The literature survey reveals that several authors were
reported in respect of the drugs under investigation. All the reported procedures found to longer run time, high injection volume and high solvent consumption under different gradient factors. These constraints make the analysis longer time and difficult to support more batches particularly in industry. No procedure or methods were found in the literature on these lines and hence investigations were devoted on zolmitriptan, rizatriptan benzoate, sumatriptan succinate, finasteride and dutasteride.

Chapter 3 reveals the development of an easy, cost-effective and time proficient stability indicating novel Isocratic reversed RP-UPLC methodology for Zolmitriptan in the occurrence of its three Impurities and humiliation products produced from forced disintegration experimentations. The Zolmitriptan was subjected to stress circumstances of water hydrolysis, thermal degradation and photolysis. The humiliation of Zolmitriptan was experimental underneath hydrolysis of acid, base and oxidation. The drug was established to be unwavering to rest of further stress environment. Attractive severance of the drug from the known Impurities and humiliation products created under stress circumstances was reached on a Acquity BEH C18,100mm X 2.1mm,1.7µm. column using mixture of ammonium dihydrogen orthophosphate adjusted to 9.5 with ammonia solution buffer and acetonitrile in the proportion of 830:170 v/v. The eluent flow rate was 0.22 mL/ min and the UV detection was at 225 nm. In the industrial liquid chromatographic methodology the resolution among Zolmitriptan and its process
related impurities i.e. impurity-1 and impurity-2 were established to be exceeding 2.0. The developed UPLC method was authenticated relating to Accuracy, Specificity, Precision, linearity and robustness. The invented UPLC technique to find out the related impurities and assay can be employed to estimate the quality of regular production and stability samples of Zolmitriptan.

The established method was simple, reliable and rapid for quantitative estimation of Zolmitriptan. The optimized comprehensive UPLC method was used to evaluate Zolmitriptan, route Impurities and Impurities created from forced humiliation experimentation. To the furthermost of our information and literature survey, the validated stability indicating UPLC methodology which took apart all the Impurities revealed in this research was not reported elsewhere.

The development of an easy, cost-effective and time proficient stability indicating novel gradient RP-UPLC method for Rizatriptan in the occurrence of its three Impurities and humiliation products created from forced disintegration studies was presented in chapter 4. The Rizatriptan was studied under different stress circumstances like acid hydrolysis, photolysis oxidation and thermal humiliation. The humiliation of Rizatriptan was found to be experimental under oxidation. When it was applied with other stress circumstances, the drug was established to be steady. Well noticeable severance of the analyte from the known Impurities and humiliation products created under stress circumstances was reached on a Acquity BEH C18,100mm X 2.1mm,1.7μm column using solution A containing
buffer i.e. 10 Mm Potassium dihydrogen orthophosphate and 2 ml triethylamine pH attuned to 3.0 with dilute orthophosphoric acid solution and solution B acetonitrile. The eluent flow rate was found to be 0.3 mL/ min and the UV detection was at 225nm. In the developed liquid chromatographic technique the resolution between Rizatriptan and its process related impurities i.e. impurity-1, 2 and 3 was found to be more than 5.0. Regression investigation proves a correlation coefficient value exceeding 0.999 for Rizatriptan and for related impurities. This methodology was proficient to detect all three impurities of Rizatriptan at a level below 0.015% with respect to analyte concentration of 0.5 mg/ mL for a 1 μL injection volume. The methodology has revealed good, reliable recoveries for Rizatriptan (99.1-100.7%) and for its three impurities (98.3-106.7). The test sample solution was established to be constant in the diluent for 48 h. The developed UPLC method was authenticated concerning Accuracy, Specificity, Precision, linearity and robustness. The developed UPLC method to find out the related impurities and assay can be utilized to estimate the quality of standard manufacture samples and stability samples of Rizatriptan.

From the experimental results it was found that the established method was trouble-free and comprehensive UPLC method to estimate Rizatriptan, process related Impurities and Impurities initiated from forced humiliation studies. It is superior method over the existing procedures/methods available in the literature.
The chapter 5 was devoted to investigate Sumatriptan for the development of an easy, cost-effective and time proficient stability representative novel gradient RP-HPLC methodology in the occurrence of its five Impurities. Further, this procedure will help to identify the humiliation products generated from forced disintegration studies. Various kinds of stress circumstances like acid, water, base hydrolysis, photolysis, oxidation and thermal degradation applied on Sumatriptan were found to be stable. The humiliation of Sumatriptan was found under base hydrolysis and acid situation. The drug was established to be stable to rest of other stress circumstances studied. A good and better resolution of severance of the drug from the known Impurities and humiliation products created under stress circumstances was found to be on a Zorbax cyano,150mm X 4.6mm,3.5 μm. column using solution A containing buffer i.e. 2.5mM orthophosphoric acid and solution B as acetonitrile. The eluent flow rate was kept 1.0 mL/ min and the UV recognition was at 225 nm. In the developed liquid chromatographic method the resolution between Sumatriptan and its process related impurities i.e. impurity-A, B, C, D and E were found to be above 1.5. Regression study confirms a correlation coefficient value exceeding 0.999 for Sumatriptan and for its related impurities. This technique was able to detect all impurities of sumatriptan at a level below 0.03% concerning analyte concentration of 0.5 mg /mL for a 1 μL injection volume. The technique has exposed good, reliable recoveries: for Sumatriptan it was 100.4.-100.6% and for its Impurities was 88.5-117.6%. The test
sample solution was established to be constant in the diluent for 48 h. The developed HPLC method was validated and found in good agreement regarding Accuracy, Specificity, Precision, linearity and robustness. The developed HPLC technique to find out the related impurities and assay can be exercised to estimate the quality of standard production samples and stability samples of Sumatriptan.

This study provides the trouble-free and inclusive HPLC method to assess Sumatriptan, process associated Impurities and Impurities initiated from forced humiliation studies. To the superlative of our information, the confirmed stability representative HPLC method which takes apart all the Impurities revealed in this research was not considered elsewhere.

Finasteride drug was investigated in view of its medicinal importance and explained in detail in chapter 6. The main focus of the current experimentation was the expansion of an easy, cost-effective and time proficient stability representative novel gradient RP-UPLC method for finasteride in the occurrence of its four impurities and humiliation products created during forced disintegration studies. The Finasteride was applied on various stress circumstances namely hydrolysis of acid, photolysis, oxidation and thermal humiliation. The humiliation of Finasteride was experiential under base hydrolysis and oxidation. The analyte was established to be stable to rest of further stress situation. A well severance of the drug from the known Impurities and humiliation products fashioned beneath stress situation was conducted on a Acquity BEH Phenyl,150mm X
2.1mm, 1.7µm column using solution A containing buffer i.e. 2.5mM orthophosphoric acid and solution B as acetonitrile. The eluent flow rate was held at 0.22 mL/ min and the UV recognition was at 210 nm. In the developed liquid chromatographic method the declaration between Finasteride and process associated impurities i.e. impurity-1, impurity-2, impurity-3 and impurity-4 was originated to be above 2.0. Regression study confirms a correlation coefficient value exceeding 0.999 for Finasteride and for four impurities. This technique was able to notice all four impurities of Finasteride at a level below 0.02% concerning analyte concentration of 0.5 mg/mL for a 1 µL injection volume. The method has revealed good, reliable recoveries for Finasteride is 99.1-100.1% and for its Impurities was 97.9-103.8%. The test sample solution was established to be constant in the diluent for 48 h. The developed UPLC method was validated with respect to method of validation constraints. Further, the developed UPLC technique is useful for the assessment of related impurities and assay of drug and its formulations.

These experimental investigations reveal that the established procedure is simple and comprehensive UPLC method to consider Finasteride, process related Impurities and Impurities originated from humiliation studies. The evaluated experimental values show that the validated stability indicating UPLC method was found to be good for generic compound along with all related Impurities.

Finally, the chapter 7 is devoted for the analytical investigation of Dutasteride which belongs to the class of drug called 5α-reductase
inhibitors. The main objective of the present study was to explore the development of an easy, cost-effective and time resourceful stability demonstrating novel Isocratic reversed phase UPLC technique for Dutasteride even in the occurrence of its three Impurities and humiliation products produced from forced disintegration experimentation. The Dutasteride was subjected to stress circumstances of hydrolysis of acid, photolysis, oxidation and thermal humiliation. The humiliation of Dutasteride was experimental under base hydrolysis and oxidation. The drug was established to be stable in the rest of other stress situations. After different experimentation, a well severance of the drug starting from the known Impurities and humiliation products fashioned beneath stress situations was finalized on a Acquity BEH C8,100mm X 2.1mm,1.7µm column using combination of potassium dihydrogen orthophosphate attuned to 5.0 with potassium hydroxide buffer and acetonitrile in the proportion of 50:50 v/v. The eluent flow rate was 0.4 mL/min and the UV detection was at 210 nm and column temperature kept at 45°C. In the invented liquid chromatographic technique the resolution among Dutasteride and process related impurities i.e. impurity-2 and impurity-3 were originated to be more than 4.0. The developed UPLC technique was authenticated with regard to Accuracy, Specificity, Precision, linearity and robustness. The invented UPLC technique to find out the related impurities and assay can be employed to estimate the quality of regular production as well as stability samples of Dutasteride.
This research work offered the simple, rapid and complete UPLC method to estimate Dutasteride, process associated Impurities and Impurities initiated from forced humiliation experimentations. To the best of our information, literature survey reveals that the validated stability indicating UPLC method was best one and not reported elsewhere.

With the above extensive experimental investigation on selective drugs, the following conclusions and recommendations are made by keeping in view parameters which will help in pharmaceutical industry and research institutions:

a) The proposed methods were cost effective, reliable, robust, less time consuming and more productive in terms of analysis of samples which are so essential for pharmaceutical industry.

b) The established procedures can be applied for routine analysis of drugs and pharmaceutical formulations.

c) The processes related impurities were separated within shorter run time and quantification of impurities resulted along with the drug substances and

d) The described analytical methods can be conveniently applied and routinely adopted to the determination of drugs in pharmaceutical formulations and bulk drugs with enhanced selectivity.

The author is cognisant of the restrictions of the approaches made and vastness of the area that still remains to be covered in this field.