ABSTRACT

Changing Requirements from ancient times to today’s fast moving century gave rise to advanced development in all the fields of science, technology, arts, etc. Various unanswered questions of old times came up with answers in the modern scientific world such as various diseases in the older times such as cancer, tuberculosis which where incurable are now having medicinal treatment. In older days the country was facing with the challenge of polio, which is now totally eliminated by proper vaccination and public awareness.

Drug Industry plays a very crucial role in this eradication of disease as it is the answer to all illness i.e. from cold, cough to severe disease. This administration of drug plays very important role in one’s life as it deals with the health issues, a dose in appropriate amount will be lifesaving while a drug with impurities can lead to severe complications. Hence monitoring of these drugs has become a vital part for pharmaceutical field.

Impurity can be defined as any substance present in the drug along with the original drug in the form of starting material, intermediates or any substance formed within the drug due to side reaction. Impurities exceeding 0.1 percent must be recognized & quantitatively determined by specific techniques. The recommended structures of the impurities, can be prepared in order to confirm the existence of these structures determined initially by spectroscopic techniques. Knowing the structures of impurities it is essential to change in order to minimize the amount of impurity with agreeable limit. Separating, identifying & determining the impurities quantitatively will help us to achieve the final product in its purest form minimizing toxicity and increasing the efficiency of drug therapy. This determination is used for drugs quality controlling & in validating of drugs as the controlling bodies such as United States Food Drug Association, current good manufacturing practice, Therapeutic Goods Administration and Medicines Control Agencies strictly focuses on the checking of debasement in the drugs.

Checking of impurity profile process starts with impurity identification by using thin layer chrom., high-performance liq. chromatography or gas chrom.. Some impurities cannot be identified by this chromatographic methods and hence requires the help of spectroscopic methods such as UV spectrometer using diode-array detector, in case of high perfor. liquid chromatography. Basic idea of impurity structure is given by NMR spectral data. Spectra obtained by the use of high-resolution & having high sensitivity NMR spectrometer & mass
spectrometer with Atomic Pressure Chemical Ionization /Environmental Science Investigation which facilitate suitably for providing the sample purity in the form of a fingerprint picture.

As per the ICH guidelines impurities less than 0.1 percent is not considered to be necessary, until these potentially present impurities are found to be unusually potent or toxic in nature.

<table>
<thead>
<tr>
<th>Degradation Product Impurity</th>
<th>Limits</th>
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<tbody>
<tr>
<td>Individual identified degraded product</td>
<td>NMT 1.0%</td>
</tr>
<tr>
<td>Individual unidentified degraded product</td>
<td>NMT 0.5%</td>
</tr>
<tr>
<td>Total degraded products</td>
<td>NMT 2.0%</td>
</tr>
</tbody>
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This thesis entitles with validation of two pharmaceutical drugs DTPEE (an antipsychotic drug, used in treatment of schizophrenia and acute manic episodes) and MPS (useful for treating urinary tract disorders & respiratory fungal infections). This methods are validated to be accurate, precise, sensitive whose results are in agreement with ICH guidelines.

First chapter Introduction deals with the general information of drug impurities, their presence due to different synthesis. Second chapter Literature Review has been reviewed to survey the work done on selected drugs and also to understand working of different techniques used for separation of precursors from APIs. The third chapter Methods and Instrumentation deals with the techniques used for validation of the drugs.

The related substances study of DTPEE was carried out by RP-HPLC method and the method is found to be validated as per recommendation of ICH guideline especially for accuracy, precision, specificity, limit of detection, limit of quantitation, linearity and range, ruggedness and Robustness parameters is briefed in chapter four named as validation of DTPEE.

Validation of MPS drug is briefed in chapter five named as validation of MPS, was carried out by RP-HPLC method along with NMR spectroscopy and the method was found to be approved as per International Conf. of Harmonization guidelines showing acceptable results for accuracy, precision, specificity, limit of detection, limit of quantitation, linearity and range, ruggedness and robustness. The drug was analyzed positively for stability study and degradation study. The reported impurities were determined, isolated and identified successfully providing a future platform for research using UPLC chromatography for their fastest recovery.

The impurities found where within acceptable limits.