CONCLUSIONS
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Quality never ends: The control of pharmaceutical impurities is currently a critical issue to the pharmaceutical industry. The presence of impurities even in small amounts may influence the efficacy and safety of the pharmaceutical products. Impurity profiling is now getting receiving important critical attention from regulatory authorities.

In the current environment of modern sophisticated equipment, great detection levels specific methods and regulatory guidance the 'quality concept' has gained the momentum. The end user of the drug product has to be assured for the quality of the medicine and thus the suitable testing of the materials is now the area of great concern. The limitations for the impurities is getting stringent day by day and at the same level, new analytical methods were developing with great detection and quantitation levels. Evolution of new chemical entities, development of new analytical methods is a never-ending process. The thirst for quality never ends.

Importance of the work: The summarized analytical development works are carried out on the basis of bulk chemical and pharmaceutical industry requirement for the suitable analytical methods for "new chemical entities".

As there is no specific analytical methods were reported in the literature in order to fulfil the requirements of bulk chemical and pharmaceutical industry. "New analytical methods' using modern High Performance Liquid Chromatographic technique were developed and are validated. These methods developed by successful use of modern 'High performance liquid chromatography' are very useful in limiting the impurities.

A new method using head-space gas chromatograph in determining the residual solvents is of great importance in the context of ICH Q3C guidelines. It gives a general method for limiting several trace residual solvents spread over the polarity index. The new method developed in determining the trace levels of 'naphthalene content' in drug intermediate or drug substance is very useful in limiting the carcinogenic impurity. The modern Gas chromatographic technique is successfully used in the cited applications.

The last but not the least the Thin layer chromatographic technique is successfully utilized in developing a suitable alternate method in place of USP described method in determining the impurity profile of Alprazolam drug substance.
Advantages:

1. **Determination of related impurities in Tamsulosin hydrochloride:** Tamsulosin hydrochloride works by blocking a specific (alpha) receptor, relaxes muscle tissue in the prostate and the opening of the bladder. Tamsulosin will not shrink the prostate; symptoms may worsen and surgery may eventually be required. Unlike most other alpha-receptor blockers used to treat benign prostatic hyperplasia (BPH), tamsulosin is not used to treat high blood pressure and hence specific for this therapeutic activity.

As per our knowledge till date there was no reported validated method in the literature for the drug substance in determining the listed possible impurities.

The analytical method developed is very simple, rapid and sensitive enough to detect all the possible potential impurities of the drug substance.

The method uses a normal ‘Spherisorb-C8’ column with simple phosphoric acid buffer with Acetonitrile (525:475 v/v, pH 3.5).

The method is sensitive enough to detect the impurities at 0.01% (0.0001mg/mL) and quantification limit of 0.025% (0.00025mg/mL).

The method is validated in the concentration range of 0.025% (0.00025mg/mL) to 0.2% (0.002mg/mL). The method is rapid enough within a short run time of 30 minutes.

2. **Determination of related impurities in Sertraline hydrochloride:** Sertraline hydrochloride is an antidepressant for oral administration. It is chemically unrelated to tri cyclic, tetra cyclic, or other available antidepressant agents. It is a novel inhibitor of serotonin reuptake in the brain.

As per our knowledge till date there was no reported validated method in the literature for the drug substance in determining the deschlorosertraline, 3-chlorosertraline and 4-chlorosertraline impurities.

The best separations were achieved within a run time of 30 minutes on a Symmetry-C18 column with a mixture of Phosphoric acid buffer (pH 3.0 with Triethylamine) and Methanol (350:650 v/v) as the optimized mobile phase.
The HPLC analytical method is validated with sufficient specificity, precision, linearity and accuracy. The method is specific in determining the structure-related impurities such as Deschloro Sertraline; 3-chloro Sertraline and 4-chloro Sertraline. The detection level is established as 0.005% (0.0001mg/ml) and the quantitation limit is established at a concentration of 0.015% (0.0003mg/ml).

3. Determination of Chiral isomer in S-Citalopram oxalate: S-Citalopram Oxalate is indicated for the treatment of major depressive disorder and maintenance therapy to prevent people with depression from suffering a relapse.

As per our knowledge till date there was no reported validated method in the literature for the drug substance in determining the chiral isomer in S-Citalopram oxalate.

A reverse phase HPLC method is developed and is suitably validated in determining the chiral isomer of the S-Citalopram oxalate drug substance.

The method uses 'Chiral AGP' column with buffer having Hexanoic acid, Tetra butyl ammonium dihydrogen sulphate, and Orthophosphoric acid in Water at pH 6.9 with Triethylamine and the buffer mixed with 2-propanol.

The method is validated over a range of 0.0025mg/mL to 0.02mg/mL. The method is validated successfully for accuracy, precision, limit of detection and quantitation levels.

The analytical method is rapid with a short run time of 30minutes, and sufficient resolution of greater than 2.0.

4. Determination of related impurities in Pantoprazole sodium: Identified the possible potential impurities of the pantoprazole sodium drug substance by the synthetic route. The analytical method is developed and is validated as per the ICH guidelines.

The method is very selective and sensitive in determining the related impurities. Established the detection capability at the lowest 0.005% (0.00005mg/mL) and quantification at 0.015% (0.00015mg/mL). Linearity is established over a range of 0.0025mg/mL to 0.002mg/mL.

The method is validated for all the other general validation parameters and is advantageous in determining the related impurities in the drug substance with the best accuracy and detection levels within a 30minutes run time, with a C18 column and disodium phosphate buffer.
5. Determination of residual solvents by Head-space gas chromatography: Although methods in determining the residual solvents were available, each method is specific with respect to the combination of solvents present.

The new Headspace gas chromatographic method is developed that covers solvents of polarity index spread over the index range from '0' to '6.6'. The combination of solvents selected is critical in separation with the spread polarity index and close boiling points.

The method developed is simple using a Wax capillary column and simple headspace chromatographic conditions. Best detection levels were achieved as low as 0.2ppm to 1ppm.

6.0 Determination of Naphthalene content by GC: Naphthalene is a carcinogenic impurity possible in drug intermediates or drug substances, which involves processing of naphthalene derivatives. Naphthalene [91-20-3] (Vol.82; 2002) is classified by The International Agency for Research on Cancer (IARC)' in group 2B under agents and groups of agents that are possibly carcinogenic to humans as evaluated in IARC monographs, and insists in controlling the impurity.

As per our knowledge till date there was no reported validated method in the literature for control of trace levels of Naphthalene.

Method capable of detecting as low as 10ppm of naphthalene content is developed and is validated. The method is accurate and precise. A use simple conventional packed SE-30 column. Short run time of 16 minutes is the added advantage.

7.0 Determination of related impurities in Alprazolam: Alprazolam drug substance is used to treat anxiety disorders and panic attacks.

The drug substance profile is described in US pharmacopoeia. However the thin layer chromatographic method described in USP is failed to in detecting the possible impurities of synthetic route under actual conditions of analysis.

Alternative analytical method using modern High performance thin layer chromatographic technique is developed and is validated. The method has an advantage of good separation, accurate determination and the best detection level as low as 0.025% (0.01mg/mL).
With all the above efforts in developing suitable analytical methods that are useful in quality evaluation of the drug substances listed, is hope useful to the bulk chemical and pharmaceutical industry for their applications.

The efforts put forward are successful in developing suitable and validated methods for the 'new chemical entities' for which no specific methods were known reported which may fulfil the industry needs.

As the bulk chemical and pharmaceutical industry is growing rapidly and at the same time under strict regulatory guidance and compliance environment, one should hope the quality at its best.