Development and Validation of New Analytical Methods for Estimation of Drugs in their Combined Dosage Forms And Validation of GC Method for Estimation of Diethylamine and 2 EHA in Ampicillin for Injection

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ABSTRACT

Objective of the research work was **"Development and validation of new analytical methods for estimation of drugs in combined dosage forms and validation of available GC method for estimation of diethylamine and 2 Ethyl hexanoic acid"**.

Recently, a new combination product (**Nuedexta Capsules**, Marketed by Avanir Pharmaceuticals) containing dextromethorphan hydrobromide (DEX) USP 20 mg and Quinidine Sulphate (QUIN) USP 10 mg has been approved by **USFDA** in **October 2010** and launched in **January 2011**. Only one method till date has been reported for simultaneous estimation of DEX and QUIN in biological fluid using Fluorescence Excitation Method. Hence, an attempt was made to develop simple, rapid, accurate and precise methods for simultaneous estimation of the both. Three methods viz., **Simultaneous equation, Derivative and RP-HPLC** methods have been **successfully developed and validated** for linearity, precision, accuracy, specificity, limit of detection and limit of quantification according to ICH guidelines.

Simultaneous equation method was performed at 226 nm and 253 nm while first order derivative at 232.6 and 245 nm in methanolic 0.5 M HCL for DEX and QUIN respectively. RP-HPLC method was developed with hypersil C8 BDS column using Phosphate Buffer (20 mM) pH 5.5, methanol and acetonitrile in ratio of 50: 40: 10 as mobile phase pumped at flow rate of 1 ml/min at 221 nm. Beer's law was obeyed in the range of 5 to 40 ppm for DEX and 2 to 16 ppm for QUIN with $\mathbf{r^2}$ **0.9991** and **0.9997** for derivative method, **0.9997** and **0.998** for simultaneous equation and 10 to 50 ppm for DEX and 5 to 25 ppm for QUIN with r^2 **0.999992** and **0.999995** respectively for RP-HPLC method. All the three methods were successfully applied to synthetic mixture spiked with standard and % recovery was found within acceptable range, which indicates potential suitability of the method for routine analysis of pharmaceutical dosage forms. All the three methods have been validated for other parameters and from the results, it can be concluded that methods are considered as **"valid".**

An attempt was made to develop Q-Ratio Method, but due to very law absorbance at Isobestic point (at 25 ppm, it showed 0.117 A) and failure to obtain linearity on repetition, the method was not further exploited.

And available **GC methods** for estimation of DEA and 2 EHA in ampicillin for injection are **suitable(valid)** for its intended use at **Astral Pharmaceutical Industries**, Vadodara, Gujarat.