Applications of Near Infrared Spectroscopy in Pharmaceutical Analysis

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SUMMARY

This thesis is concerned with the implementation of Near Infrared technology in pharmaceutical analysis. The recent developments in the international standards and regulatory requirements make it essential to improve the daily analysis routine to achieve 100% inspection to, at least, all the raw materials introduced in the pharmaceutical products while, in the same time, maintain maximum safety, prevent any source of cross contamination between materials and comply, fully, with the GMP guidelines.

This thesis is tackling three main issues, of special concern to pharmaceutical manufacturers, regarding the daily routine of raw material analysis, these issues are; Identification and Qualification (Particle Size Grading), Differentiation between physically and chemically similar materials as well as excluding the effect of packaging plastic bags while performing the NIR analysis. The aim is to ensure rapid and accurate analysis that makes the 100% inspection of raw materials possible in a fast and safe manner with no need for direct sampling or performing several analyses for identification and qualification of those raw materials.

Three main experiments were performed; the first, *Qualification of Ibuprofen Powder Grades*, aims at the identification and qualification of different Ibuprofen grades. Ibuprofen is supplied to the pharmaceutical industry in two main grades; the 20 microns grade and the 40 microns grade. Usually differentiation between the two grades is carried out using *Particle Size Analysis Methods* which are time consuming and they are usually coupled with a prior identification method. In addition, these conventional methods of analysis cannot be performed for all the containers of every single batch of Ibuprofen Material supplied to the factory. Instead, using FT-NIR technology solves these three problems; where both identification and particle size qualification can be done at a single scan, the speedy and non destructive advantages of the NIR technique enables a pharmaceutical factory to perform 100% analysis for all the containers of all the batches supplied to the factory, which in turn adds to the factory compliance to GMP and new international standards and requirements.

The second method, *Differentiation of Parabens*, aims at the differentiation of the family of para-hydroxybenzoic acid esters, *the parabens*, which are widely used in the pharmaceutical industry as preservatives; this method is going to differentiate between 3 members of the parabens family; Methyl Paraben, Methyl Paraben Sodium Salt and Ethyl Paraben Sodium salt. It is clear that these materials have very similar chemical structure and subsequently very similar spectra, and here is the challenge to develop a chemometrical differentiating method that maximize the spectral difference between those similar materials and to be selective, specific and precise in differentiating the members of that family. The method will depend on the fact that the NIR spectra is dominated by the overtones and combinations of C-H bonds in addition to a minor contribution of second overtone of the C=O vibrations, so the model will try to intensify the spectral difference and the discriminatory power of the frequencies that are affected by both the length of the ester and the para-hydroxy group. Also the model should be designed in a way to overcome any effect of the physical differences between the materials (like particle size or what so ever) so that the method is sensitive only to differences in the chemical structural.

The third method, *Effect of Plastic Bag on the differentiation of Aromatic Amino Compounds*, aims at the differentiation of three Aromatic Amino Compounds, which is a family of amines and amides that are widely used in the pharmaceutical industry as active ingredients, especially in the drugs for cold and flu; this method is going to differentiate between 3 amines and amides; Ambroxol HCl, Paracetamol and Caffeine Anhydrous. These materials have amino compounds of different spectral behavior, the challenge is to develop a chemometrical differentiating method that maximize the spectral difference between those similar materials while excluding the effect of the packaging plastic bags and to be selective, specific and precise in differentiating these classes. The method will depend on the fact that the NIR spectra is dominated by the overtones and combinations of C-H bonds and N-H bonds in addition to a minor contribution of second overtone of the C=O vibrations, so the model will try to intensify the spectral difference and the discriminatory power of the frequencies that are affected by both the degree of the amine and the amide (*primary, secondary* or *tertiary*). Also the model should be designed in a way to overcome any effect of the plastic bag and the physical differences between the materials so that the method is sensitive only to differences in the chemical structural.

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