Near infrared transmittance analysis for the assay of pharmaceutical tablet and Multivariate Analysis

Abstract
This paper is a case study illustrating how the active substance in pharmaceutical tablets can be quantified from NIR spectroscopy data using multivariate methods like Principal Component Analysis (PCA) and Partial Least Squares Regression (PLS), as these techniques can remove the high degree of redundancy seen in NIR data. A variety of spectroscopic data pre-treatment methods are applied to separate information from noise, like classical scatter correction techniques, as well as the more recently developed extension, called extended multivariate scatter correction. It will be shown that the choice of pre-treatment is crucial to success, especially since NIR data is often subject to light scatter.

Introduction
The Process Analytical Technology (PAT) initiative promotes the pharmaceutical industry to perform large-scale quality control analysis on a routine basis. Such analysis requires fast and reliable measurement techniques in combination with multivariate data analysis.

Near Infrared (NIR) spectroscopy has gained considerable attention in recent years due to speed and the fact that no special sample preparation is needed. In addition, NIR spectroscopy is a nondestructive measurement device, and has successfully been applied in many areas of production in the chemical industry. Since typical NIR spectra are not readily interpretable compared to other spectroscopic techniques, multivariate analysis of the spectroscopic data is required to build quantitative models.

Material and Methods
The samples used were Escitalopram coated tablets of four different dosage values (5, 10, 15 and 20 mg in dose proportional tablets). Samples were collected at pilot, Full scale and Laboratory studies. 10-15 tablets from each dosage value were used for the study. NIR Transmittance spectra were collected at pilot, Full scale and Laboratory studies. 10-15 tablets from each dosage value were used for the study. NIR Transmittance spectra were recorded in the range 700-2500 nm from each tablet. Traditional analysis of Assay content analysis has been performed by using HPLC. The Unscrambler was used to develop regression model for the assay content of the Escitalopram tablets. The different preprocessing techniques were applied and comparative analysis done. Below (fig:1, fig:2, fig:3) are the screenshots of different pre-processing techniques applied over data.

Results and Discussions
Initially Partial Least Square Regression (PLS) were applied to the complete range of spectrum i.e. 700-2500 nm and also different data range were created from 1100 – 1250 nm and developed PLS methods. Below (fig:4) is the scores plot which clearly shows the variability in the dosage forms as well as different studies.

Second approach of the data analysis is PLS Model is applied over the spectral region of only 1100-1250 nm with out preprocessing the data. This Model required 3 PC’s to explain the most variation in the data with RMSEC of 0.35

Conclusion
Different approaches were considered in the process of method development.
• From the different calibration models the PLS Regression model with Multi Scatter Correction (MSC) for the spectral range 1100-1250 nm were prove to be good one with number of principle components 2 with RMSEC of 0.33. Below is the comparative study chart of different preprocessing techniques.

• From the scores plot, it was clear that the lab study was more similar to the full scale than the pilot study.

<table>
<thead>
<tr>
<th>Preprocessing</th>
<th>Data set</th>
<th># PCs</th>
<th>RMSEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>All</td>
<td>5</td>
<td>0.35</td>
</tr>
<tr>
<td>None</td>
<td>Region</td>
<td>3</td>
<td>0.35</td>
</tr>
<tr>
<td>MSC</td>
<td>All</td>
<td>3</td>
<td>0.34</td>
</tr>
<tr>
<td>MSC</td>
<td>Region</td>
<td>2</td>
<td>0.33</td>
</tr>
<tr>
<td>1st derivative</td>
<td>All</td>
<td>5</td>
<td>0.38</td>
</tr>
<tr>
<td>1st derivative</td>
<td>Region</td>
<td>1</td>
<td>0.38</td>
</tr>
<tr>
<td>2nd derivative</td>
<td>All</td>
<td>3</td>
<td>0.36</td>
</tr>
<tr>
<td>2nd derivative</td>
<td>Region</td>
<td>3</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Acknowledgements:
Martin Kermit, CAMO Software AS – Næsby Vallagan, 8 – NO-0158 Oslo- Norway  martin.kermit@camo.no
Sunil Kumar B.V, CAMO Software India Pvt. Ltd., Domlur Layout, Bangalore, India  skumar@camo.co.in

Suresh Kumar B.V , CAMO Software India Pvt. Ltd., Domlur Layout, Bangalore - 560 071
Fax: +91 (80) 4125 4181
Tel: +91 (80) 4125 4242

CamO Software India Pvt. Ltd., 14 & 15, Krishna Reddy Colony, Domlur Layout, Bangalore - 560 071
INDIA
Tel: +91 (80) 4125 4242
Fax: +91 (80) 4125 4181