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TO STUDY THE ANALYSIS OF SOLID ORAL DOSAGE FORMS INCLUDING THE DIFFERENT MODERN ANALYTICAL TECHNIQUES

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Abstract: Solid oral dosage forms provide a highly reproducible and convenient form of drug delivery. Generally easy to manufacture and stable, they are the most common form of self-medication. When Solid oral dosage forms is incorporated into polymers that are used to modify its physical state or control its release in the gastrointestinal tract. These formulations often present considerable challenges to the pharmaceutical chemist. Different techniques are utilized for the analysis of the solid oral dosage form. The one which is used in the modern times are Microscopy, X ray Powder Diffractions, Thermal Analysis, Fourier Transform Infra Red (FTIR) Micro spectroscopy, Nuclear Magnetic Resonance (NMR) Imaging, Near-Infrared (NIR) Analysis, Raman Spectroscopy.

Keywords: Overview of Analysis of Solid oral dosage forms including X ray Powder Diffractions, Fourier Transform Infra Red (FTIR) Micro spectroscopy, Nuclear Magnetic Resonance (NMR) Imaging.

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INTRODUCTION

Analysis of oral solid dosage forms

Introduction[1]

- Solid oral dosage forms provide a highly reproducible and convenient form of drug delivery. Generally easy to manufacture and stable, they are the most common form of self-medication.
- Immediate-, controlled-, and extended release solid oral dosage forms are easy to manufacture reproducibly and provide convenient delivery systems for self-administered medications.
- To design an effective delivery system, it is important to know the physical state of the API in the dosage form.
- When it is incorporated into polymers that are used to modify its physical state or control its release in the gastrointestinal tract. These formulations often present considerable challenges to the pharmaceutical chemist. Solid oral dosage forms are designed to deliver the drug through physiological mechanisms that preside throughout the gastrointestinal tract.
- To design an effective delivery system, it is important to know the physical state of the API in the dosage form; therefore, this chapter will focus to a large extent on the solid-state aspects of the solid oral dosage forms.
- Tests that demonstrate that the state of the API within the dosage unit is in specified physical form increase the dependability and understanding of product.
- To facilitate the development of immediate, controlled, and extended release and other types of solid dosage forms, noninvasive and nondestructive *in situ* techniques provide insight into the physical nature and micro homogeneity of the dosage form.
- Solid oral dosage forms are designed to deliver the drug through physiological mechanisms that preside throughout the gastrointestinal tract.

Techniques of Analysis: [3, 4, 7]

- Different techniques are utilized for the analysis of the solid oral dosage form. The one which is used in the modern times are as mentioned follow.

1. Microscopy.
2. X ray Powder Diffractions.
3. Thermal Analysis.
4. Fourier Transform Infra Red (FTIR) Micro spectroscopy.
5. Nuclear Magnetic Resonance (NMR) Imaging.
6. Near-Infrared (NIR) Analysis.
7. Raman Spectroscopy.

Microscopy

- Light microscopy, PLM, SEM, and transmission microscopy are nondestructive techniques that can provide insight into the composition and homogeneity of the API throughout the dosage form.
- These techniques lead to understanding and a prediction of the dosage form's performance characteristics, such as the dissolution profile, ruggedness of the product.
- Potential flaws in the coating that imparts the controlled-release characteristics to the product**.**
- Different techniques that are utilized to determine how an API is distributed within granulation are;

Optical microscopy (1-150µm)

Electron microscopy (0.001µm)

- For submicron particles it is necessary to use either:

TEM (Transmission Electron Microscopy) or

SEM (Scanning Electron Microscopy).

TEM and SEM (0.001-5µm)

PLM and energy-dispersive X-ray spectroscopy

- A polarized light micrograph of cross section of the granulation matrix is shown in Figure 1.
- Crystals of the intact API are plainly visible within the matrix. Because the API is a hydrochloride salt, energy-dispersive X-ray spectroscopy, an elemental analysis technique, was used to map chlorine content (Fig. 2) and reveal the distribution of the API in the granulation. These experiments demonstrate that the API exists as the hydrochloride salt in the granulation and retains its original particle size distribution; therefore, the high temperatures and drying conditions used in the manufacturing process do not appear to have negatively affected the drug substance.

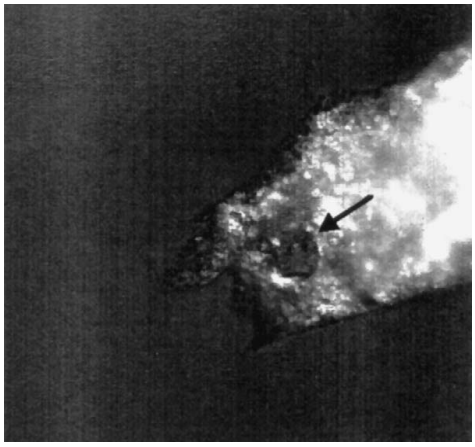


Figure 1

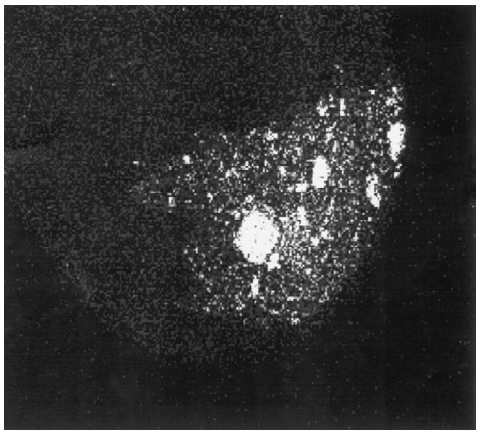


Figure 2

Figure 1: Polarized light micrograph of a granulation. Crystals of the API (see arrow) are visible within the matrix of the granulation.

Figure 2: Chlorine mapping of a granulation containing a hydrochloride salt API.

X ray Powder Diffractions

- It is used to detect crystalline compound-lattice.
- A collimated beam of X-rays is incident upon this lattice, X-rays are diffracted.
- Every crystal own characteristic X-ray diffraction pattern.

Technique is useful for:

- Distinguishing between solid-state forms of a bulk drug substance.
- Distinguishing between polymorphs, hydrates, and solvates.
- Characterizing changes in the drug substance in a solid state as it exists in a matrix of a formulation.

For example, a change from a crystalline to an amorphous form or hydration, dehydration, etc.

Thermal Analysis

- Thermo-gravimetric and differential thermal analysis (TG/DTA) are useful techniques for the solid-state characterization such as :

Determinations of loss on drying,

Phase transition temperatures,

Thermal stability, and

Water is bound or unbound.

Idea about storage condition.

- The TG/DTA data are derived from the response of the sample to a heating program. In DTA the sample temperature remains constant throughout an endothermic transition, whereas the sample temperature increases during an exothermic transition.
- A TG curve is simultaneously acquired, yielding the corresponding mass change curve. These dual pieces of information make interpretations more straightforward than interpretation with either technique alone.

- TG/DTA was utilized to monitor changes in the crystal morphology and physical changes of a hydrated API in a granulation blend and in tablets compressed from the blend.

Fourier Transform Infra Red (FTIR) Micro spectroscopy

- It is useful technique for the identification of the compound.
- It utilizes small sample for the analysis.
- When unidentified crystalline particles were found growing on tablets during a stability study, FTIR micro spectroscopy with a spectral resolution of about 5 µm was used to chemically analyze and identify the minute particles.
- FTIR spectrum of excised crystals found on tablets during a stability study.
- The crystals were identified as stearyl alcohol.
- Infrared spectroscopy is well established, and infrared spectra are considered to be definitive for identity testing in the pharmaceutical industry. FTIR micro spectroscopy, equipped with an automated stage, is a nondestructive technique that can be utilized to analyze small samples and to chemically map locations by identifying components within the sample.

Nuclear Magnetic Resonance (NMR) Imaging

- To understand structural changes that occur in controlled-release dosage forms as they interact with physiological fluids.
- E.g. Hydroxypropyl methylcellulose (HPMC) tablets that form a gel layer when the polymer matrix hydrates and swells.
- NMR imaging techniques were used to measure self diffusion coefficients (SDCs) of water across the gel layer.

Raman Spectroscopy

- Determination of solid-phase physical properties of the API in different solid dosage forms.
- E.g. used to analyze solid dispersions to evaluate the physical properties and determine the distribution of ibuprofen in extrudates of polyvinylpyrrolidone (PVP).
- The lack of any further Raman shifts during a stability study indicated that the ibuprofen in the melt extrudate is stable and that there were no crystallization processes that could affect the dissolution and bioavailability.
- Therefore, one use of Raman spectroscopy could be to optimize various formulations.

Near IR (NIR) Spectroscopy

- There is intense interest in using NIR techniques in several major areas of

pharmaceutical operations: clinical supply identification, incoming raw material.

Qualitative NIR Analysis

Verification of the Identity of Packaged Clinical Supplies

- NIR analysis is particularly suited to the verification of the identity of packaged clinical supplies because of its nondestructive nature, speed, and low-cost. Because every clinical study is a unique event consisting of a finite population of dosage forms, models can easily be generated and validated, and the final-blinded products can be tested the same day that the analysis request is made.
- An NIR spectroscopic method to identify pharmaceutically active and Inactive (placebo) clinical dosage forms were recently developed.
- Typically, the dosage form is packaged with its placebo in the same blister pack. The purpose of the NIR identification method was to identify, nondestructively and rapidly, the four forms in the blister pack. The method was developed to create and validate a one-time-use library of the spectra of clinical dosage forms prepared for double-blind clinical trials.
- A novel approach was used to generate and validate the library simultaneously.
- In pharmaceutical tablet production, one of the key measurements of productqualityis the standard active content uniformity test. This provides measure of uniformity of the blend from the assay of a number of tablets (typically 10) taken from the tablet press. The test usually involves dissolving the tablet forHPLC and only the active contents measured. However, the tablet comprises a number of other ingredients.
- Known that these ingredients can impact important product properties such as dissolution (amajorregulatoryconcern at the moment), stability, bio-availability and various process-quality parameters such as hardness.

Raw Material Identification

- Currently, the primary use of NIR for pharmaceutical analysis is in the identification of raw materials.
- Some regulatory agencies have mandated that100% of the materials to be released for use should be verified, rather than the use of traditional statistical sampling, before the materials are mixed and compounded in production.
- If NIR is utilized to comply with this mandate, a 1997 European Pharmacopoeia monograph, which specifies the minimum standards for an

NIR identification method, should be consulted.

- The spectral variations from an average spectrum of a raw material represent the variation that may be encountered in the future.
- The library is dynamic, as it can be updated to incorporate new raw materials, raw materials whose physical characteristics have changed, or phased-out raw materials that are no longer used in the manufacturing process.
- Constructing a library composed of mean spectra and their variances allows many different compounds to be stored, and the spectrum of an unknown material is matched against all possible similar compounds.
- The unknown is either accepted or rejected based upon how close (within accepted variations) its spectrum matches that of a known compound.

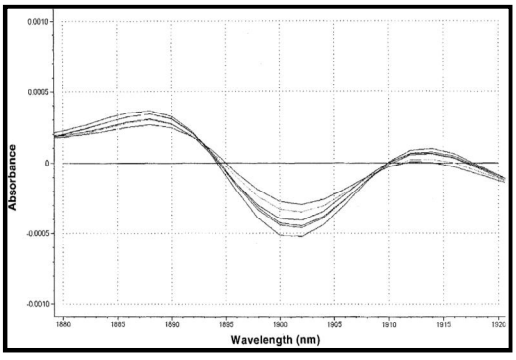


Figure 3**: NIR** spectra at high, middle, and low positions of a V-blender after 1 minute of mixing.

Blend Homogeneity

- In one study, the homogeneity of pharmaceutical raw materials during blending was followed by visual matching, spectral matching, or principal component analysis of the spectra after discrete time intervals.37
- In another study, the feasibility of the use of NIR spectroscopy at-line during production to control product quality was examined.38 NIR spectra obtained after different mixing intervals were used to assess the extent to which four components were blended in a V-blender.
- NIR reflectancspectrawerecollected with the use of a fiber-optic probe at “high,” “middle,” and “low” positions on the blender at 1, 5, 10, 15, and 20-minute intervals

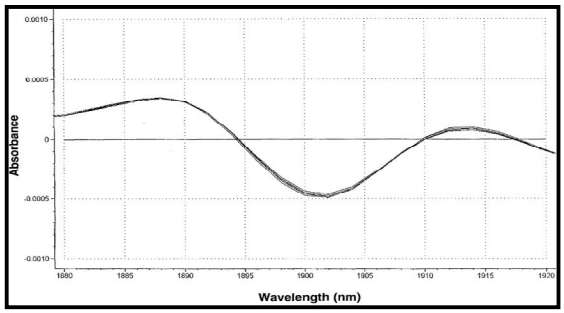


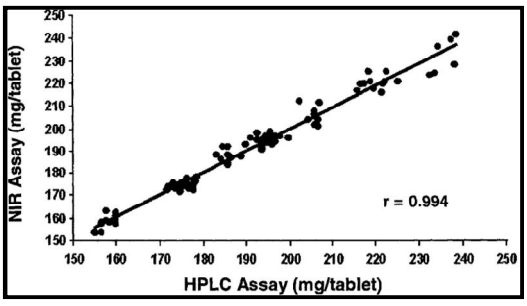
Figure 4: NIR spectra at high, middle, and low positions of a V-blender after 20 minutes of mixing.

Quantitative NIR Analysis

- The need for both automation and high-speed analysis in the analytical

laboratory has already been addressed. One technique that seems to combine the best of both is NIR analysis. Once an NIR assay is validated, an analyst cans generate single-unit analyses usually in less than 1 minute per sample. In a single morning, dozens (possibly hundreds) of single-unit analyses can be performed and reported.

- The use of American Society for Testing and Materials (ASTM) standards was proposed to assist in the validation of NIR spectroscopic methods.
- Currently, there are no existing regulatory guidelines for validating a NIR method. The ICH validation guidelines for analytical methods and othercompendial guidelines were integrated with ASTM standards to satisfy regulations and validate a quantitative NIR transmission assay for tablets.
- What is significant about these studies is that they independently arrived at the same conclusions regarding their approach for validating NIR methods for the analysis of pharmaceutical products.



- NIR methods can be validated by the conventional protocols described in ICH and other regulatory guidelines as they are currently written.
- some modifications have to be made to account for differences between spectrophotometricand chromatographic experimental parameters
- For example,
- Spiked recovery experiments are not relevant because NIR responses are sensitive to the production process. The criteria suggested for validating a NIRtransmission method.
- Specificity Principal Component analysis (PCA) for identification. Accuracy Residual analysis, difference of the estimated (NIR) value from the reference value, from ASTM Standard E 1655.

REFERENCES

1. USP 24, pp. 299–301. U.S. Pharmacopeia Convention, Rockville, MD, 1999.

2. Indian Pharmacopoeia-2007, Government of India, Ministry of Health & Family Warfare, New Delhi. Volume-1. Page No.177-83.

3. Ahuja S., Scypinski S, “Handbook of Morden Pharmaceutical analysis”, Volume 3, Academic Press, New York. Pg No. 235-252.

4. http://www.horiba.com/scientific/products/particle-characterization

5. CVS Subrahmanyam," Textbook of physical pharmaceutics" vallabh prakashan, Delhi. Page No.220.

6. Lechman L, "Theory and practice of industrial pharmacy", 3rd adition, Varghese publication house. Page No: 453-475.

7. Brittain Harry G," Spectroscopy of pharmaceutical solid"volum-160. Page no-192-227.