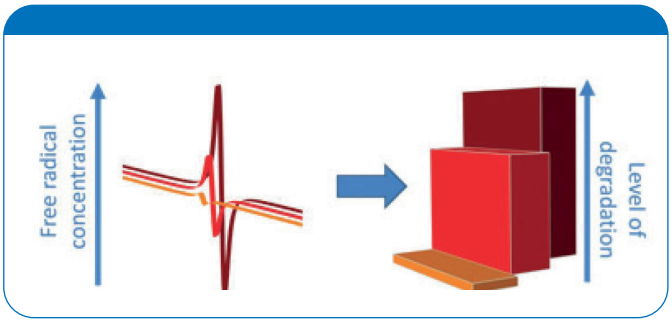
Pharmaceutical Applications of EPR

I. Detecting and Evaluating Degradation

Therapeutic drugs require a well characterized shelf-life to ensure correct dosage and patient safety. Developing successful formulations depends on a thorough understanding of their chemical and physical stability and properties.

Heat, light, oxygen, moisture, sterilization processes, impurities, and excipient interactions are some of the factor that can compromise product stability. Moreover, all these factors may cause degradation of the active pharmaceutical ingredients (APIs), excipients, or formulations resulting in loss of product potency or toxic by-product generation. Degradation processes quite often involve free radicals and transition metals that are responsible for the majority of the damage that occurs in drug products.

Electron Paramagnetic Resonance (EPR) spectroscopy is the only technique for the direct and non-invasive detection of unpaired electrons in paramagnetic species (free radicals and transition metals). By analyzing an EPR signal, one can identify, quantify and monitor temporal behavior of the free radicals involved in product degradation.



Degradation correlates with the EPR signal

Challenge

Chemical stability of pharmaceutical molecules is a matter of great concern as it affects the safety and efficacy of drug products.

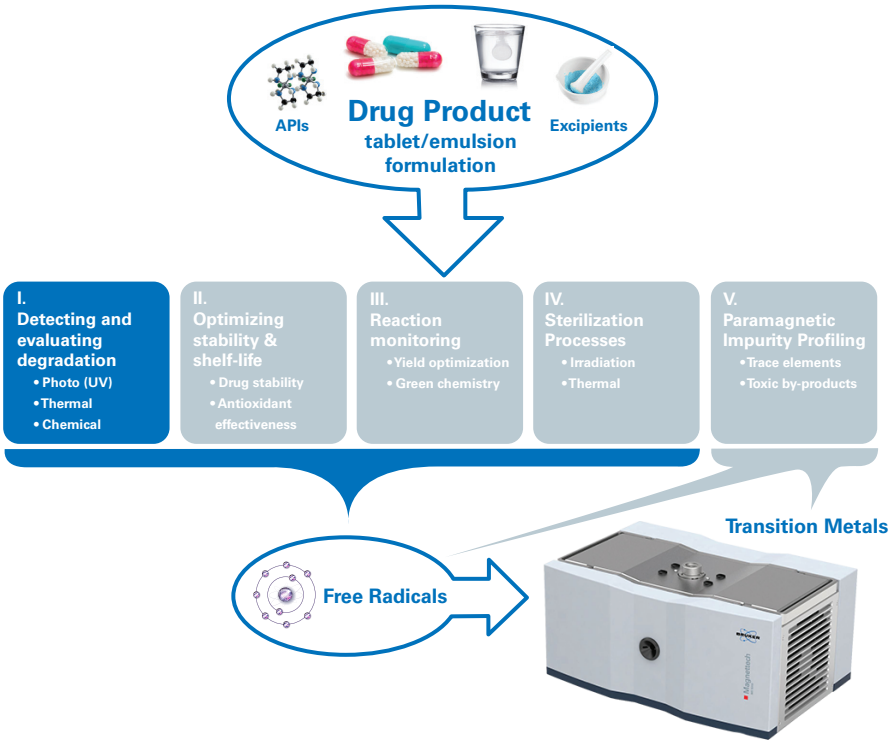
Solution

The Bruker EPR spectrometers

- Determine the root causes of degradation in drug products
- Measure the extent of degradation of APIs, excipients, and formulations
- Predict long-term stability characteristics of the APIs, excipients and formulations

EPR portfolio key features:

- Accurate results
- Superior sensitivity and high resolution
- Ease of use
- Full workflow for measuring, analyzing and quantifying free radicals
- Bench-top model with a compact footprint
- Floor-standing systems for state of the art pulse EPR
- Full range of accessories and options
- Quantitative package with SpinFit and SpinCount

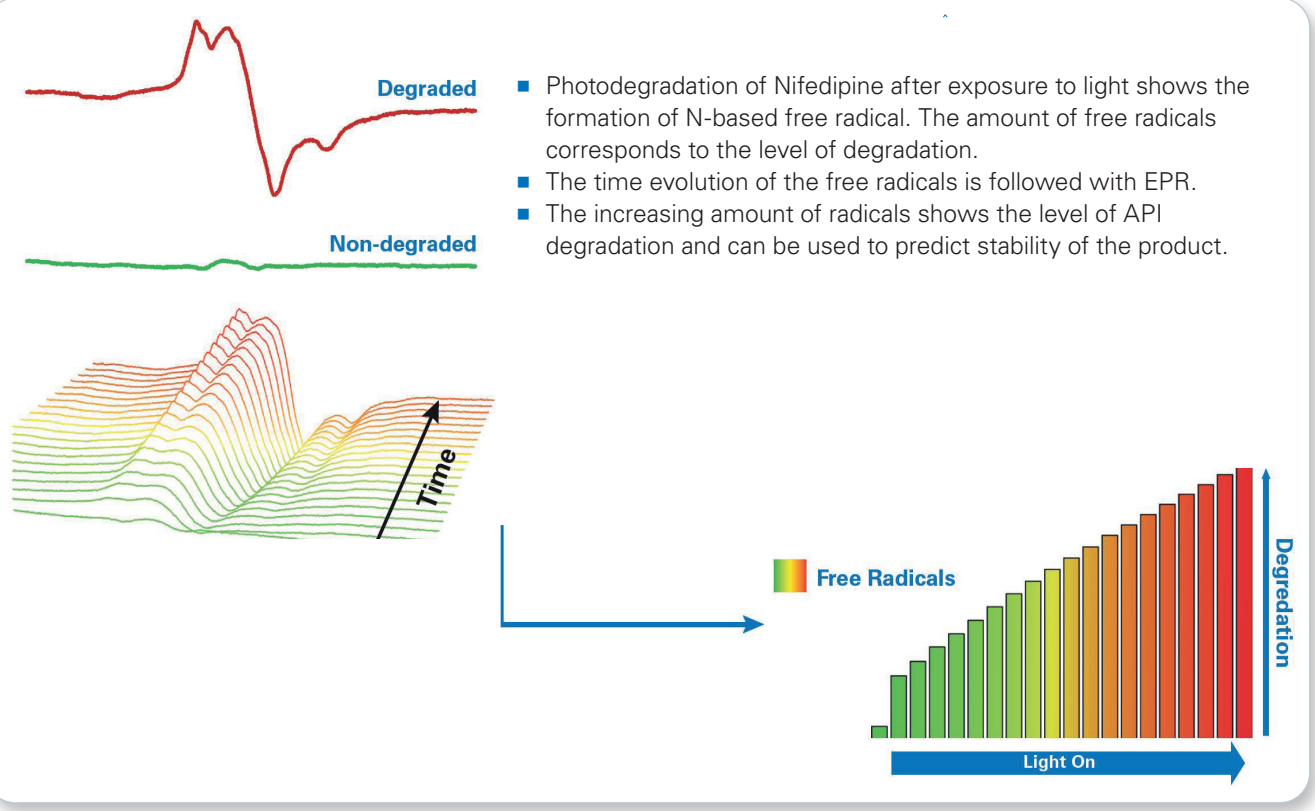


Summary

Understanding degradation of APIs, excipients, and their interactions is crucial for drug product safety. The Bruker EPR spectrometers (bench-top and floor-standing) are the solution to investigate the stability of pharmaceutical products. With EPR one gains insights into the degradation mechanism so you can optimize product stability.

References

1. Williams H. et. al. (AstraZeneca), The power of electron paramagnetic resonance spectroscopy in pharmaceutical analysis , Spectroscopy Europe (2006) 18(1)
2. Williams H. et. al. (AstraZeneca), Predicting the photostability characteristics of active pharmaceutical ingredients using electron paramagnetic resonance spectroscopy, Drug Dev. Ind. Pharm. (2012) 38(2) 200
3. Mangion I. et. al. (Merck), Using electron paramagnetic resonance spectroscopy to facilitate problem solving in pharmaceutical research and development. J. Org. Chem. (2016) 81 6937



- Photodegradation of Nifedipine after exposure to light shows the formation of N-based free radical. The amount of free radicals corresponds to the level of degradation.
- The time evolution of the free radicals is followed with EPR.
- The increasing amount of radicals shows the level of API degradation and can be used to predict stability of the product.

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