Pharmaceutical Applications of EPR

II. Optimizing Stability and Shelf-Life

Forced degradation (stress testing) is routinely used in pharmaceutical development to predict the stability of drug products that affects purity, effectiveness, and safety. In stress testing the drug product is exposed to heat, light or chemical agents with the goals being:

- understanding degradation pathways
- determining the intrinsic stability and shelf-life
- developing stable formulations
- evaluating antioxidant efficiency

Product degradation often involves a free radical pathway therefore identifying the radical intermediates is extremely important. In addition, antioxidants' efficiency in drug formulations is characterized by the ability to scavenge the free radicals and eliminate stability issues.

Electron Paramagnetic Resonance (EPR) spectroscopy can successfully detect and monitor short-lived free radicals produced during stress testing via chemical, thermal, or photochemical reactions. EPR can determine radical scavenging effectiveness and efficiency of antioxidants.

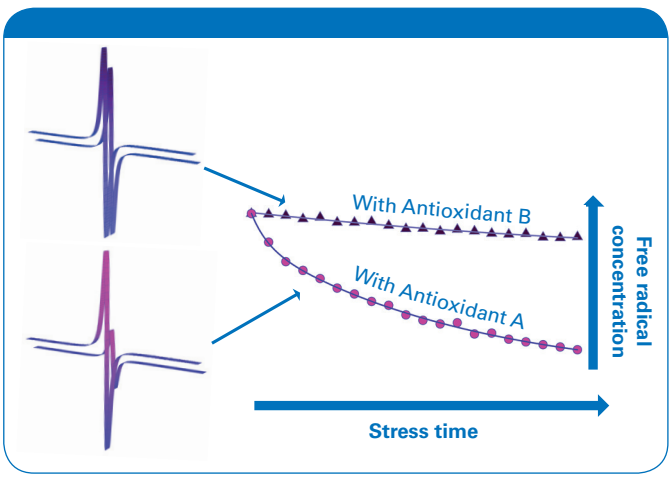
Challenge

Knowledge of stability and shelf-life of APIs and excipients is required for selecting a proper drug formulation. Stress testing is required by ICH guidelines.

Solution

The Bruker EMXnano benchtop EPR spectrometer package

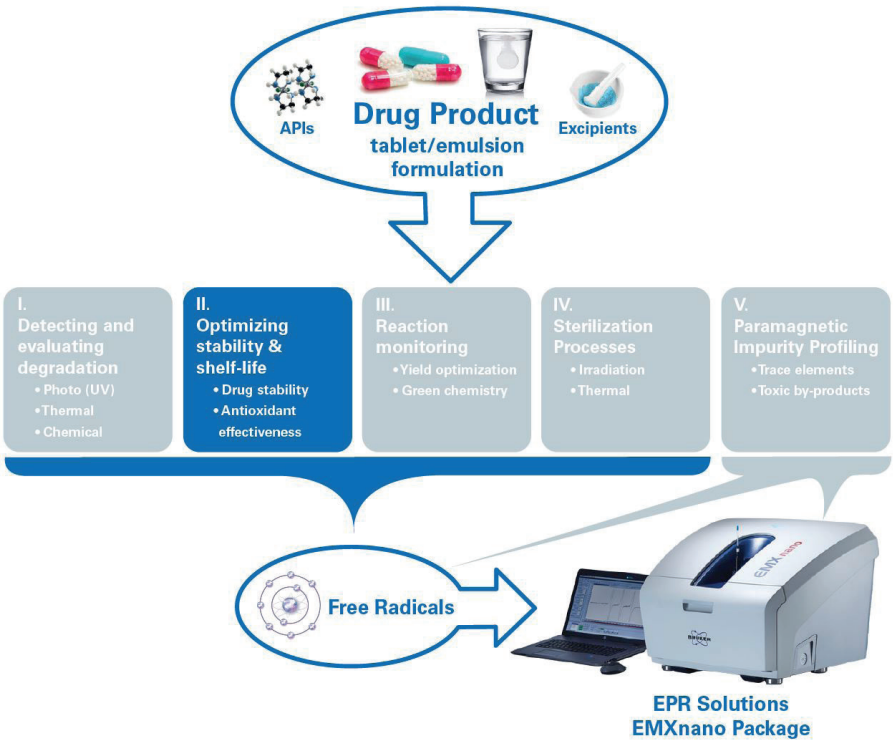
- Predicts long-term stability (photo-, thermo-, chemical) of drug products by monitoring processes that produce and involve free radicals
- Uses minimal sample quantities in early development phase of new APIs
- Determines the antioxidant efficiency to quench free radicals with well established assays



Antioxidant A is more effective than antioxidant B at quenching the free radicals in the drug formulation

EMXnano key features:

- No prior EPR experience needed
- Video how-to-guide and startup kit
- Accurate results
- Superior sensitivity
- Ease of use
- Full workflow for measuring, analyzing and quantifying free radicals
- Compact foot print
- Low cost of ownership

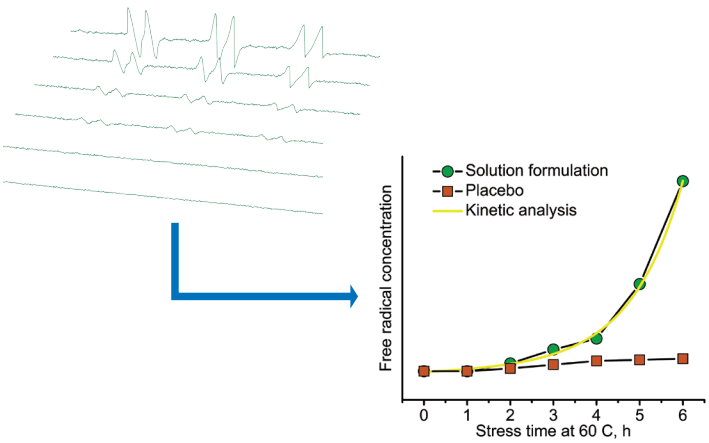


Summary

Forced degradation studies are essential in the drug formulation process providing knowledge of possible degradation pathways. The EMXnano provides data to predict the stability of APIs, excipients, and formulations. EPR stress studies provide the necessary insights to aid in choosing an appropriate formulation in early development phases.

References

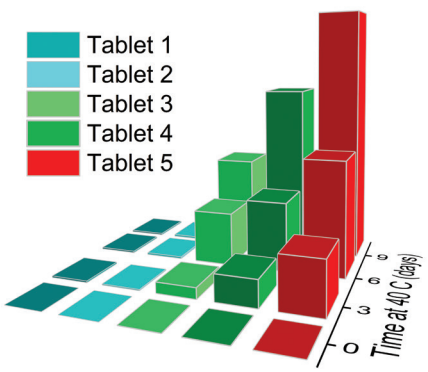
1. Williams H. et. al. (AstraZeneca), Predicting the photostability characteristics of active pharmaceutical ingredients using electron paramagnetic resonance spectroscopy, Drug Dev. Ind. Pharm. (2012) 38(2) 200
2. Carini et al., Electron paramagnetic resonance (EPR) spectroscopy: a versatile and powerful tool in pharmaceutical and biomedical analysis, Curr. Pharm. Anal. (2006) 2 141
3. Persich et al., "Dark" singlet oxygen and electron paramagnetic resonance spin trapping as convenient tools to access photolytic drug degradation, J. Pharm. Sci. (2017) in press



- Solution formulation undergoes thermal degradation via a free radical process.
- Temporal analysis provides rates of oxidation.
- Data with placebo confirm that the API is susceptible to degradation on heat exposure.

Case study: Shelf-life

- Five tablet formulations stress tested at 40 C over a time course of 10 days.
- Increasing free radical formation detected in tablets 3-5 indicates a reduced shelf-life.
- Tablets 1 and 2 with low radical formation have better potential for drug development.



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