Pharmaceutical Applications of EPR

IV. Sterilization Processes

APIs, excipients, final drug formulations, laboratory equipment, and medical devices, may need to go through a sterilization process. The most commonly used sterilization methods are: gamma or electron beam irradiation, dry heat, and pressured vapor sterilization.

However, all of these sterilization processes can generate free radicals:

- Free radicals are responsible for the degradation of the irradiated materials
- Free radicals cause alteration of the physico-chemical properties of the sterilized product
- Free radicals decrease drug potency by partial decomposition during sterilization
- Free radicals may be a toxicological hazard

Electron Paramagnetic Resonance (EPR) spectroscopy is the only technique for the direct and non-invasive detection of free radicals. By quantifying free radicals, one can assess the level of degradation during sterilization processes.

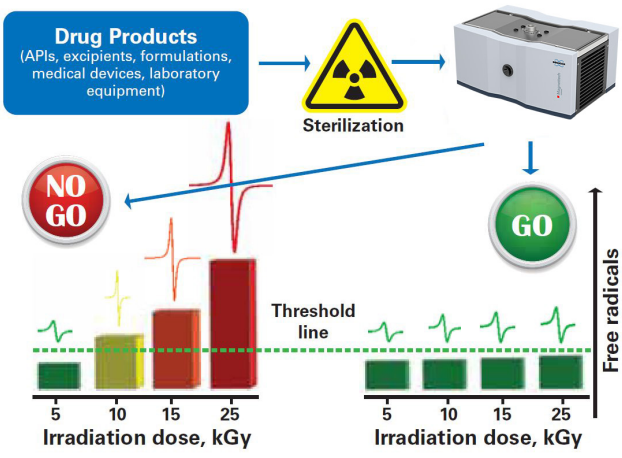
Challenge

Sterilization processes can be responsible for drug inactivation or alteration of functional excipients and APIs.

Solution

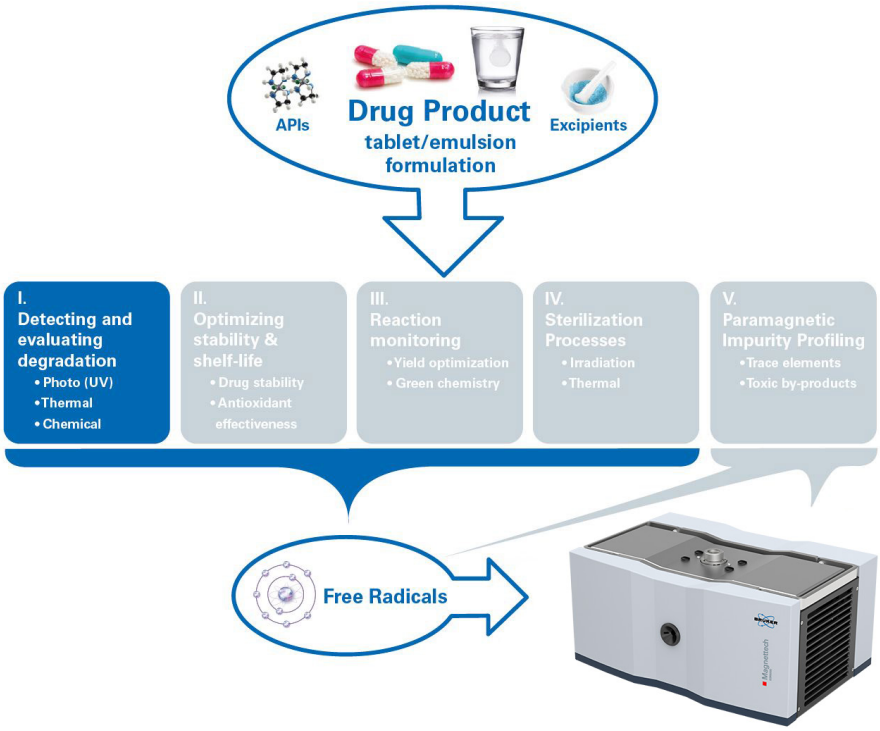
The Magnettech ESR5000 benchtop EPR spectrometer package

- Determines stability of drug products after sterilization
- Characterizes free radicals and identifies their source
- Provides easy 'go/no go' decisions based on quantification of free radicals for quality control and assurance (QC/QA)



Magnettech ESR5000 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



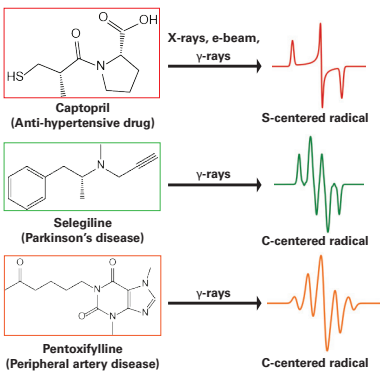
Summary

EPR complements the many methods used to analyze sterilization effects. Specifically it investigates the role of free radicals in the degradation of pharmaceutical products.

Evaluation and necessary optimization are easy to perform using a Magnettech ESR5000. The ability of the instrument to detect, identify and quantify free radicals in post-sterilized drug products makes it suitable not only for R&D laboratories but also for QA/QC facilities.

References

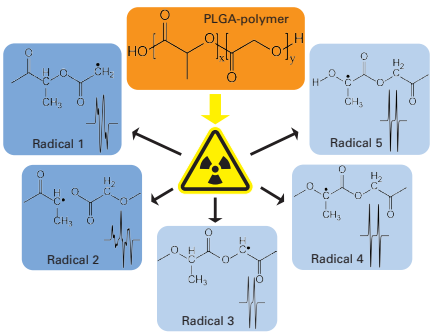
1. Bushell J.A. et al. (Astra Zeneca), An EPR, ENDOR a,d EIE study of γ-irradiated poly (lactide-co-glycolide) polymers. Magn. Reson. Chem. (2006) 44 929
2. Bushell J.A. et al. (Astra Zeneca), An EPR and ENDOR study of γ- and β-radiation sterilization in poly (lactide-co-glycolide) polymers and microspheres. J. Control. Release (2005) 110 49
3. Engalytcheff A. et al., Attempts at correlation of the radiolytic species of irradiated solid-state captopril studied by multi-frequency EPR and HPLC. Radiat. Res. (2004) 162 616
4. Köseoglu R. et al., Electron paramagnetic resonance of some γ-irradiated drugs. Appl. Radiat. Isot. (2003) 58 63



- Gamma-irradiation of drugs in the solid-state (Captopril, Selegiline, Pentoxifylline) induces S-centered or alkyl free radicals.
- Identifying the structure of radicals provides a better understanding of the mechanism of radiolysis.
- Quantification of radical amount enables you to establish a threshold for the radiosterilization of these drugs.

Case Study

- Sterilization via γ-irradiation causes degradation and morphological changes to the excipient poly (lactide-co-glycolide) PLGA-polymer.
- The degradation of PLGA occurs through chain scission reactions producing 5 different radicals.
- The relative concentration of these radicals varies depending on the annealing conditions.
- Radicals 1 and 2 dominate at low temperatures (77 – 120 K) whereas the more stable radicals 3, 4, and 5 are found at 250 – 300 K.



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