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Microscopy in Glass Corrosion Analysis of Parenteral Products

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Most injectable pharmaceutical products (parenterals) are packaged in glass vials or syringes. Glass is an ideal packaging material due to its chemical compatibility with most parenteral products. There are, however, some parenteral products that can induce or accelerate glass corrosion processes [1]. Glass corrosion can result in the generation of glass particulates in the drug product which is clearly undesirable. There is an expectation by regulatory authorities that pharmaceutical manufacturers will understand the propensity of their product to cause corrosion and to monitor corrosion on accelerated stability studies. Various optical and electron microscopy techniques have been applied to this problem along with several other analytical methodologies [2].

It is convenient to categorize the various applicable analytical techniques by those that examine the vial contents or the vial itself. These examinations can look for evidence of glass particles in the liquid or evidence of glass corrosion on the interior surface of the vial both before and after emptying. It is useful to examine the vial contents using stereomicroscopy with oblique illumination and examine the vial interior with differential interference contrast optical microscopy (DIC) before removing the contents. This initial examination has two objectives: 1) determine whether there is evidence of severe corrosion; 2) establish the shape and morphology of particles and surface defects before the vial contents are emptied.

Confirmatory tests for glass corrosion include filtration and SEM/EDS of the collected particles, inductively coupled plasma spectroscopy (with either optical emission spectroscopy or mass spectrometry), and SEM examination of the interior glass surface. Figure 1 presents a DIC image of a corroded vial interior before removal of the liquid contents. Figure 2 presents a corresponding SEM image of the same glass interior after removal of the liquid contents. The filigree pattern on the interior is characteristic of glass corrosion.

There are a number of confounding factors to accurate assessment of glass corrosion. First, there are a variety of different glass corrosion mechanisms yielding different kinds of particle generation and different corrosion patterns [1]. These mechanisms will depend upon the type of vial glass, the method of vial manufacture, vial cleaning, and the nature of the liquid in the vial – particularly pH. Figures 1 and 2 present the most common features associated with glass attack. In some cases, though, the attack is more uniform across the surface and can only be detected by high resolution SEM. In some cases, the glass flakes resulting from corrosion have typical conchoidal fracture whereas in other cases, the large visible particles are actually agglomerated small ones. In some cases, elemental analysis using ICP will detect increased Si content with glass attack and, in other cases, it will not. One must also be careful to ensure that the evidence of glass attack corresponds with glass corrosion and not a result of inadequately cleaned vials or poorly manufactured ones.

In conclusion, various microscopy techniques are an indispensable component of the assessment of glass corrosion but one must be careful to integrate all of the evidence in order to make an accurate judgment.

REFERENCES

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[2] Diebold KJ, Modern Microscopy Journal (web), 2003 pp. 1-15.

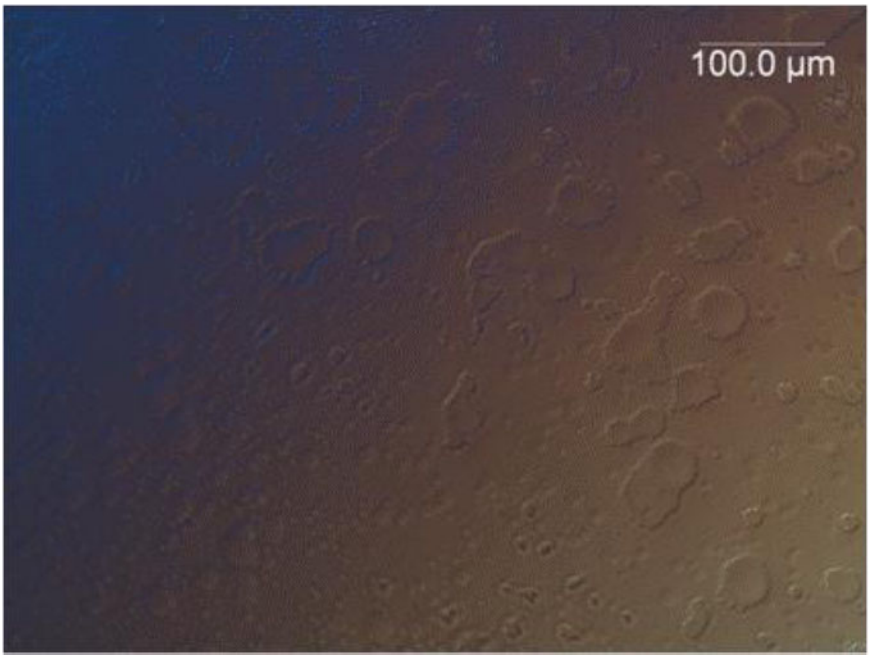

Fig. 1 DIC Image of Corroded Glass Vial

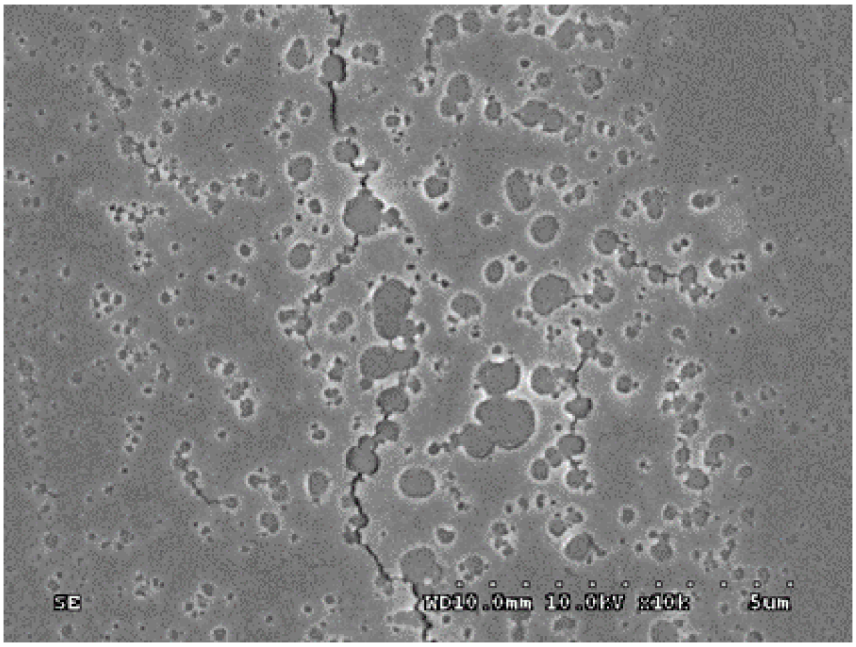

Fig. 2 SEM Image of Corroded Glass Vial

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