Solid State Pharmaceuticals: Thermal and Photo- Stability

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Drugs degrade to different extents on separate exposure to heat, moisture, oxidation and light. A combination of these stresses may result in complex behaviour [1,2]. Thermal stability is the simplest to assess, generally by use of the techniques of thermal analysis (TA) [3-5]. Comparison of TA experiments done using inert and oxidising atmospheres provides information on the susceptibility of the drug to oxidation. Addition of controlled amounts of water vapour to the purge gas allows a quantitative study of hydrolysis. The photostability of a drug substance however, will depend upon the wavelength, the intensity and the time of exposure to the radiation, as well as a variety of physical factors such as the type, shape and orientation of the sample holder. These factors are all incorporated in the radiation dose, which is usually determined by actinometry using a standard sample [6,7]. From a practical point-of-view, the conditions used for thermal and photostability testing may be far removed from those to which a typical drug substance or drug formulation will be exposed. It can however be presumed, that if the substance is stable under the exaggerated conditions, it will not be affected by lesser stresses.

In reviewing the literature to obtain possible correlations between the results of thermal and photochemical studies on the same substances in the solid state, one encounters several difficulties. There are many results for the photodegradation of substances in aqueous solution, but relatively few studies are done of photostability in the solid state. Correlations between photochemical behaviour in solution and in the solid state are not always clearly established. In aqueous solution, the temperature range of thermal degradation studies is very limited and hydrolysis is likely to be a major competitive process. There are also many studies where drugs have been reported as being stable to both heat and light. For example, Suleiman et al. [8] reported that, in the solid state, diltiazem is highly stable to high humidity with added exposure to UV light, even though aqueous solutions hydrolyse relatively rapidly.

The criterion for literature selection has thus been that this study should report on the photo- and/or thermal stability of one or more of the solid forms of the following drug substances: carbamazepine, cianidanol, furosemide, nifedipine, mefloquine, St John's wort and tolbutamide. Behaviour may obviously be complicated by the existence of several polymorphic forms. Where possible the photolytic behaviour has been compared with any thermal information. In some cases the photochemical behaviour in aqueous solution has provided additional insights.

The stability of drugs towards heat, moisture, oxidation and exposure to light is a topic of great practical interest and any degradation will usually adversely affect the therapeutic activity of the drug. Unless very special precautions are taken, most drugs will receive some exposure to light and will generally be expected to be able to tolerate room temperature. One of the interesting questions that arises in considering drug stability, and which is discussed here, is the possible correlation between thermal degradation and photodegradation.

In the solid state, the temperatures required for thermal degradation at a measurable rate are generally far higher than the temperatures existing, even locally, during photolysis, so the mechanisms of thermal and photochemical degradation can be expected to differ.

Attention has been focused on the solubility of polymorphic active ingredients and the influence of polymorphism on dissolution kinetics and bioavailability [9]. Since most drugs exhibit polymorphism, it is the goal of the pharmaceutical manufacturer to develop the most thermodynamically stable polymorph to ensure the bioavailability of the product over its shelf-life [10]. However, it is also their task to formulate a product which is physically and chemically stable and to this end the thermal and photostability of different polymorphic forms of drug substances is important. Although it is difficult to compare the thermal and photostability of drug substances in the solid state, this study [11-18] highlights the fact that various crystal forms of drug substances, exhibit not only different thermal behaviour but also different photostability.

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