Desiccants for Pharmaceutical Applications

Desiccants are a critical part of the pharmaceutical process chain. The correct selection and use of a desiccant can prevent many problems occurring and ensures the integrity and performance of finished products, as this article illustrates.

Ian Buckley* is the business development and export sales manager and **Alan Newbold** is the sales and marketing director at Silgel Packaging Ltd, UK.

*To whom correspondence should be addressed.

Desiccants are materials that adsorb and retain water vapour. Most desiccants are solids that contain a network of interconnected pores that allow water molecules to become attached to the large internal surface. The concentration of water vapour in air is expressed as relative humidity (RH), which is defined as the ratio of the amount of water vapour present in air to the maximum amount of water vapour that can be held in the air at a given temperature.

RH, which is expressed as a percentage, and temperature are important factors during the production and packaging of intermediates and finished drugs. In addition to air, packaging materials can also act as a source of moisture. Desiccants reduce the amount of water vapour in air and prevent unwanted damage.

Moisture and Pharmaceuticals

The quality and appearance of some pharmaceutical intermediates, preparations and finished medicines depends substantially on the protection afforded by dessicants. Moisture is one of the most damaging forces in drug production and using some form of protection against water vapour is vital to good product presentation, integrity and performance. The importance of the little sachet or plastic canister inside the bottle or foil pouch should not be underestimated.

Moisture Damage

Moisture damage can take many forms. If left alone, moisture retained in containers and other packaging can cause many problems. Common examples include

- degradation of active intermediates
- reduction in drug potency
- reduction in tablet hardness
- discolouration
- smeared tablet print
- development of unpleasant odours
- growth of mould and mildew.

Desiccant Types

The principal desiccants used in pharmaceutical applications are silica gel and molecular sieve. Silica gel is available in two main types: a white, non-indicating version and one that changes colour when moisture is adsorbed. The latter is obviously useful to indicate when the desiccant is used up.

Self-indicating gels also have a number of varieties, the older blue-to-pink gels and the more recent yellow-to-green ones. Blue-to-pink gels contain cobalt chloride so are subject to legislation in Europe that requires a toxic hazard label. Yellow-to-green gels do not pose such health and safety issues.

White-to-pink gels are also available but these contain phenolphthalein, a known carcinogen.

Molecular sieve is a special type of desiccant that can reduce moisture levels to almost zero. Such desiccants are available in different pore sizes with varying capacities for moisture adsorption. Molecular sieve is used in specific applications where moisture needs to be completely removed.

Activated carbon, while not a desiccant, is often used to absorb odours. A general comparison of the properties of different desiccants is given in Table 1.

Desiccant Sachets

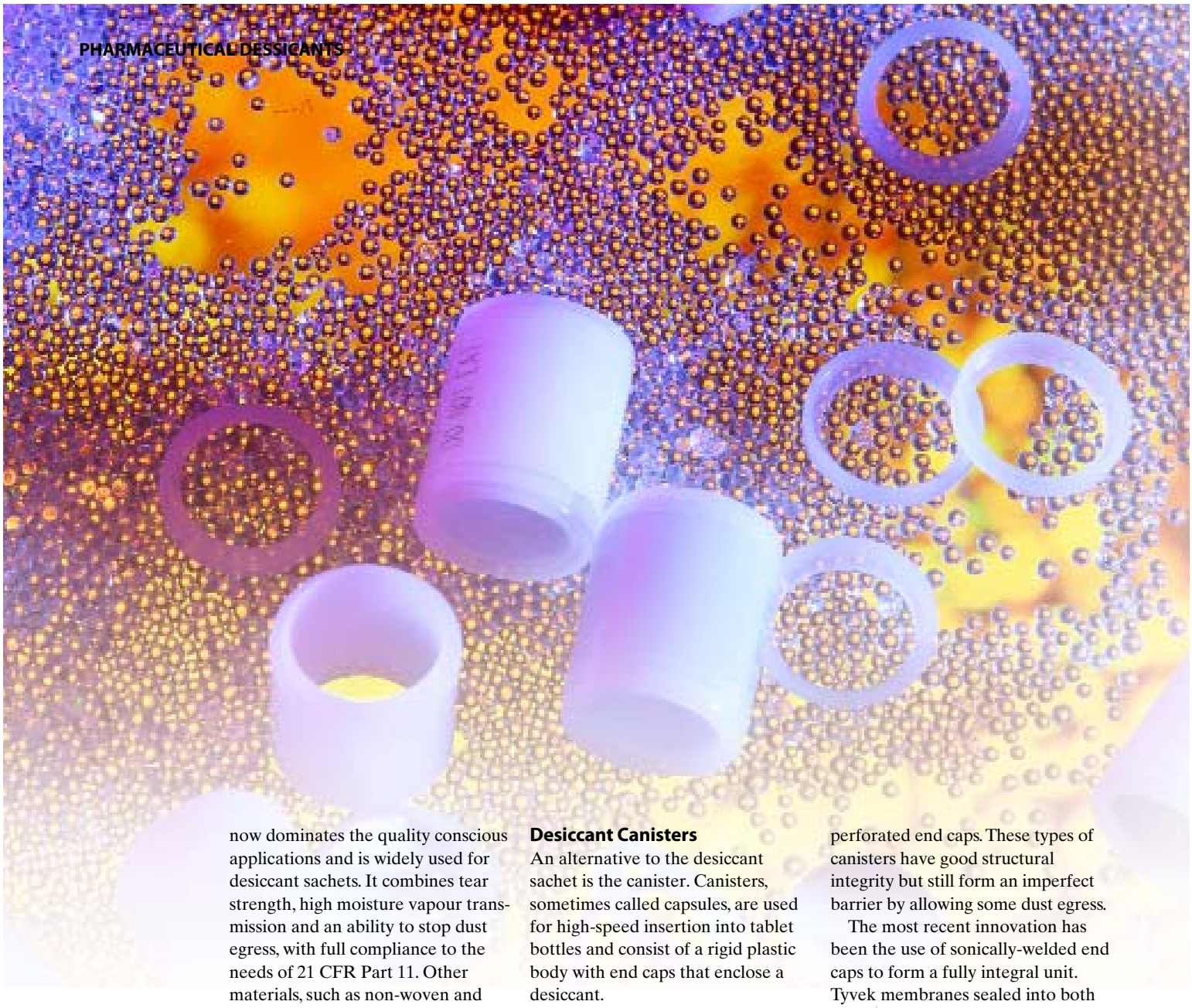
Desiccants are presented in a variety of forms, shapes and sizes. The most common form is a sachet presented as a single unit. Sachets also vary in size from 0.25 grams up to 2.5 kilogrammes of desiccant depending on the application.

Sachet materials play a critical part in desiccant performance and acceptability for pharmaceutical use. DuPont's *Tyvec* is a material that

As with all pharmaceutical materials, desiccants are required to meet strict quality assurance and performance criteria. Desiccant suppliers are subject to regular quality management system audits by pharmaceutical companies to ensure that high standards are met.

Table 1 A general comparison of desiccant properties.

Property	Silica gel	Molecular sieve
Occurrence	Synthetic — made from sodium silicate and sulfuric acid	Synthetic zeolite
Composition	Hydrous silica $SiO_2.nH_2O$	Potassium/sodium aluminosilicate
Structure	Amorphous porous solid with interconnected pores	Crystalline porous solid with uniform network of internal cavities connected by pores
Form	Beads or granules	Beads
Surface area (m^2/g)	>800	700–800
Average pore diameter (Å)	Approximately 20	Available in specific pore sizes: 3A – 3 4A – 4 13X – 10
Health and safety	Non corrosive and non-toxic	Non corrosive and non-toxic
Form after moisture adsorption	Non swelling, remains dry	Non swelling, remains dry
General adsorption rate	Good overall rate but rapid above RH 30%	Good adsorption rate, excellent at low RH
Adsorption at normal temperatures	Extremely efficient	Extremely efficient
Adsorption at high temperatures	Poor	Excellent
Adsorption capacity at low RH	Poor	Excellent
Adsorption capacity at high RH	Excellent	Fair
Adsorption rate at high RH	Excellent	Poor
Adsorption capacity at 30°C and 60% RH	Excellent	Fair



now dominates the quality conscious applications and is widely used for desiccant sachets. It combines tear strength, high moisture vapour transmission and an ability to stop dust egress, with full compliance to the needs of 21 CFR Part 11. Other materials, such as non-woven and paper are also available. A semi-translucent material from DuPont, *Teijin*, is often used to show the colour change of indicating gels. This also conforms to the requirements of 21 CFR Part 11.

A comparison of the properties of different sachet materials is given in Table 2.

Desiccant Canisters

An alternative to the desiccant sachet is the canister. Canisters, sometimes called capsules, are used for high-speed insertion into tablet bottles and consist of a rigid plastic body with end caps that enclose a desiccant.

Certain types of older canisters have a card insert in one end only, which provides moisture transmission through a single end. The card-enclosed canisters have a tendency to pop open if squeezed, allowing desiccant to escape. These problems were addressed with the development of rigid bodied canisters with porous or perforated end caps. These types of canisters have good structural integrity but still form an imperfect barrier by allowing some dust egress.

The most recent innovation has been the use of sonically-welded end caps to form a fully integral unit. Tyvek membranes sealed into both ends of a high density polyethylene (HDPE) canister body provide the combination of dust-free sealing, moisture transmission and integrity of construction. Canisters can be automatically inserted into bottles at high speed and provide high production efficiencies with the optimum level of moisture protection.

Table 2 General comparison of properties of sachet materials.

	Tyvek	Teijin	Non-woven	Paper
Material	Polyethylene	Polyethylene/ polyethyleneterephthalate	Viscose	Paper pulp
Moisture vapour transmission	Very good	Very good	Excellent	Very good
Non-dusting	Excellent	Very good	Good	Fair
Comments	Best to use	Use with self-indicating silica gel	May release loose fibres	Inexpensive

Canisters can contain both desiccants and odour adsorbing materials such as activated carbon or mixtures of both. Another recent application involves the use of oxygen adsorbers in canisters.

Safety Requirements

The commonly used desiccants meet the legislative requirements to use with pharmaceuticals.

Silica gel, an amorphous solid, is the desiccant most often used in pharmaceutical applications. It is made by the reaction of sulfuric acid with sodium silicate to produce a hydrous gel, which is then dried to form a glass-like material with an open pore structure.

A common misconception is that amorphous silica gel shows the same properties as the crystalline mineral silica, which is a potential carcinogen. Mineral silicas contain quartz but amorphous silica gels do not and therefore do not have the associated health and safety issues.

Silica gel meets international standards of purity for food use and, according to the United Nations FAO/WHO, has an unlimited allowable daily intake (ADI). It is also listed in A1 of the List of Additives in the *Codex Alimentarius*. In the US, amorphous silica gel is listed for pharmaceutical applications in the US Pharmacopoeia.

Molecular sieve, another commonly used desiccant, is the synthetic analogue of a naturally occurring zeolite mineral. Synthetic zeolites are aluminosilicates with interconnected pores and chambers, and are listed under the relevant sections of 21 CFR and the GRAS list.

Sachet and canister materials also generally meet the requirements of 21 CFR. Most of the available canisters have an FDA drug master file (DMF) number. DMF numbers are increasing in importance for desiccants, particularly in Europe, where they are becoming a requirement for canisters.

Quality Issues

As with all pharmaceutical materials, desiccants are required to meet strict quality assurance and performance criteria. Desiccant suppliers are subject to regular quality management system audits by pharmaceutical companies to ensure that high standards are met.

An ongoing requirement is also that suppliers show good waste and environmental management practice. This is often demonstrated by accreditation to BS EN ISO 14001, the environmental management system standard.

Before a desiccant product can be used in pharmaceutical applications, it must show consistency in terms of both its manufacture and its technical performance. Long-term stability trials are often performed along with production validations between suppliers and users. ■