ICS 11.120.99
CCS 10

G r o u p s t a n d a r d s

T/CNPPA XXXX-20XX

Guidelines for classification and application of medicinal desiccants

(Draft for soliciting opinions online)

XXXX-XX-XX Release XXXX-XX-XX Implementation

Released by the China Pharmaceutical Packaging Association

catalogue

Preface

This document is drafted in accordance with the provisions of GB/T 1.1 2020 "Guidelines for Standardization Work Part: Structure and Drafting Rules of Standardization Documents".

Please note that certain contents of this document may involve patents. The publishing institution of this document does not assume the responsibility of identifying patents.

This document is proposed and under the jurisdiction of the China Pharmaceutical Packaging Association.

Drafted by:

The main drafter of this document by:

Introduction

As an auxiliary packaging component, medicinal desiccants are an important means of controlling moisture during the storage period of drugs. Medicinal desiccants are commonly used in oral solid preparations and are also applied in other drug formulations, such as the use of antibiotic products filled in powder-liquid double chamber bags. With more desiccants being applied in pharmaceuticals, the current standards for medicinal desiccants only include silica gel and molecular sieve desiccants, and only specify the quality parameters ,lacking comprehensive description and selection guide for medicinal desiccants used in the pharmaceutical industry. Therefore, developing selection and evaluation standards for medicinal desiccants is necessary to help pharmaceutical companies better understand and choose medicinal desiccants, to ensure drug quality.

This standard describes the elements involved in selecting desiccants, e.g. safety and functionality. Safety is an important evaluation element when selecting medicinal desiccants, adding desiccants to drug packaging systems should not introduce new risks. Safety assessment includes assessing the safety of the desiccant itself and the impact of desiccant packaging materials on drug safety. On the basis of meeting drug safety requirements, appropriate desiccants and desiccant packaging are selected based on the moisture requirements during drug storage, combined with the functional characteristics of various desiccants (such as the water absorption rate of desiccants).

This standard summarizes the types and packaging systems of current medicinal desiccants, and proposes the selection principles and evaluation elements when using desiccants in drugs.

Guidelines for classification and application of medicinal desiccants

1 Range

This document specifies the basic classification, selection, and application methods of medicinal desiccants.

This document is applicable to guiding pharmaceutical companies to choose suitable medicinal desiccants based on the needs and characteristics of drugs.

2 Normative reference documents

The contents of the following documents constitute essential provisions of this document through normative references in the text. Among them, only the version corresponding to the date of the referenced document is applicable to this document; The latest version (including all modification orders) of the referenced document without a date is applicable to this document.

Chinese Pharmacopoeia 5902 General Rules for Solid Medicinal Desiccants (Draft for Comments)

GB/T 41897-2022 Quality Requirements for Food Desiccants

BB/T 0049-2021 Packaging desiccants

T/CNPPA 2001-2017 Oral solid pharmaceutical high-density polyethylene non-woven bag desiccant

3 Definition and terminology

3.1 Desiccant

A product that can absorb moisture through physical and/or chemical reactions, reduce the humidity inside the corresponding sealed packaging to a certain level, and maintain it for a certain period of time.

3.2 Specific surface area

The surface area of a solid substance per unit mass.

3.3 Saturation moisture absorption rate

The moisture absorption rate measured after the desiccant adsorbs water vapor to

equilibrium.

3.4 Moisture content

The percentage of weight loss of a known desiccant after drying at a specified temperature for a certain period of time compared to the initial weight of the desiccant.

3.5 Sealed packaging of desiccants

Container or packaging material for placing desiccants. This packaging can prevent contaminations of dust or foreign matter , with certain degree of semi transparency.

4 Classification and performance of medicinal desiccants

4.1 Classification of desiccants

Medicinal desiccants are classified according to the material of the desiccant.

4.1.1 Silicone desiccant

Silicone desiccant is usually a sheet-like or granular material made by reacting sodium silicate with sulfuric acid, undergoing a series of post-treatment processes such as aging and acid foaming. Silicone is an amorphous substance with a transparent and irregular spherical shape, and its chemical formula is $mSiO_2 \cdot nH2O$. Silicone desiccant is a highly porous structure of hydrated silica, which is non-toxic, odorless, and odorless. Silicone desiccant is makes a highly active adsorbent material with stable chemical properties and strong hygroscopic properties,. The commonly used silicone desiccants include type A and type B. The specific surface area of type A silicone is between 650-800m^2/g, and the specific surface area of type B silicone is between 400-550m^2/g. The larger the specific surface area, the stronger the moisture absorption ability.

4.1.2 Molecular sieve desiccant

Molecular sieve desiccants are microporous aluminosilicates in the form of flakes or particles. According to various pore size, commonly used molecular sieve desiccants include models 3A, 4A, 5A, and 13X. The chemical formula of 3A molecular sieve is 2/3K2O • 1/3Na22O • AI2O3 • 2SiO2 • 9/2H2O, and the adsorbed molecules must be less than 0.3nm. The chemical formula of 4A molecular sieve is $Na_2O \cdot Al_2O_3 \cdot 2SiO_2 \cdot 4.5H_2O$, and the adsorbed molecules must be less than 0.4nm. The chemical formula of 5A molecular sieve is $3/4CaO \cdot 1/4Na_2O \cdot Al_2O_3 \cdot 2SiO_2 \cdot 4.5H_2O$, and the adsorbed molecules

must also be less than 0.5nm. The chemical formula of 13X molecular sieve is Na2O • Al2O3 • 2.45SiO2 • 6.0H2O, with a pore size of 10A, and can adsorb molecules larger than 3.64A but smaller than 10A.

4. 1. 3 Activated carbon desiccant

Activated carbon is a type of microcrystalline carbon material with a black appearance, odorless, non-toxic, well-developed internal pore structure, large specific surface area, and strong adsorption capacity processed from carbon containing materials (such as coconut shells and charcoal). Activated carbon desiccants can be divided into powder and granular shapes according to their shape. The most commonly used type is refined granular carbon, with specifications including 5g, 10g, 15g, 30g, 50g, etc. The specific surface area of activated carbon desiccants usually reaches 1000m^2/g, which not only absorbs moisture but also adsorbs odors.

4. 1. 4 Fiber desiccant

A desiccant made from natural plant fibers, coated with PET and cut.

4. 1. 5 Others

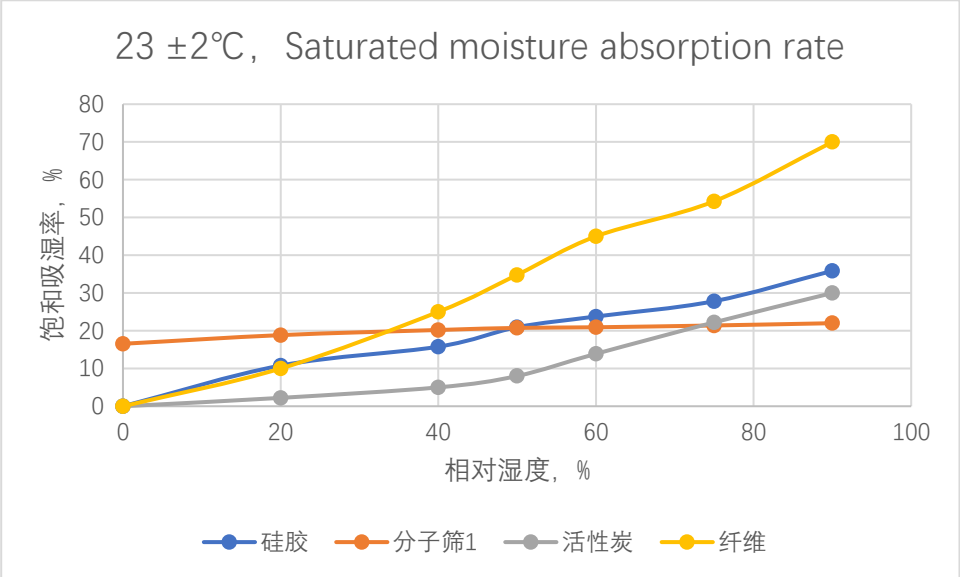
Mixed desiccant, a desiccant made from two or more different materials. For example: silicone-molecular sieve desiccant mixed desiccant; Siliconeactivated carbon desiccant, etc.

4.2 The characteristics and application of desiccants

4. 2. 1 Moisture absorption performance of desiccants

The moisture absorption performance of different types of desiccants varies under different temperature and humidity conditions. At room temperature (23 ± 2 ℃), the moisture absorption performance of different types of desiccants under different humidity conditions is as follows (see Figure 1).

Figure 1: Saturated moisture absorption rate of desiccant under different humidity conditions at 23±2℃



4. 2. 2 Application of desiccants

The characteristics of different types of desiccants vary, and there are also certain differences in their applications. The main characteristics and applications of each type of desiccant are shown in the table below:

Table 1: Characteristics and Applications of Different Desiccants

Desiccant type	characteristic	application
Silicone desiccant	Under the same temperature and different humidity conditions, the saturation moisture absorption rate of silicone desiccants changes significantly. The moisture absorption capacity of silicone desiccants is greatly affected by environmental humidity. Silicone desiccants release a small amount of water molecules into the environment after moisture absorption saturation.	The most suitable hygroscopic environment for silicone is room temperature (20-32℃) and high humidity (60-90%), which can reduce the relative humidity of the environment to about 10%.
Molecular sieve	The moisture absorption capacity of molecular sieve desiccants is less	The most suitable hygroscopic environment

desiccant	affected by environmental humidity. Under the same temperature and different humidity conditions, the saturation moisture absorption rate of molecular sieve desiccants does not change significantly. Molecular sieve desiccants can not only adsorb water vapor, but also other gases. Under low temperature and low humidity conditions, molecular sieve desiccants have excellent moisture absorption performance, and the moisture is difficult to desorb after absorption, which can maintain the environmental humidity at an extremely low level.	temperature for molecular sieve desiccants is 0-32 ℃, and the relative humidity is 0-30%.
Activated carbon desiccant	The moisture absorption capacity of activated carbon desiccants is greatly affected by environmental humidity. Activated carbon desiccants have strong water absorption and also possess the ability to produce odors.	Activated carbon desiccants are suitable for use under medium to high humidity conditions, with a hygroscopic environment temperature of room temperature~32℃.
Fiber desiccant	The moisture absorption capacity of fiber desiccants is greatly affected by environmental humidity. Fiber desiccants have a fast moisture absorption rate and high moisture absorption rate.	The saturated moisture absorption rate can reach 100% of its own weight (25℃, RH=100%), which is three times that of ordinary silicone desiccants; The surface of fiber desiccant is

		coated with film and can be cut or punched into various shapes, or directly filled into bottle caps or other containers.

5 Sealed packaging of desiccants

5.1 Requirements for sealed packaging of desiccants

The common forms of sealed packaging include bags, bags, columns, pipes, cans, drums, combination covers, etc. The packaging materials used include paper, LDPE, HDPE, PP, composite materials, etc. The sealed packaging of desiccants directly comes into contact with drugs, and it is necessary to choose safe and suitable packaging materials. The sealed packaging of desiccants should meet the following requirements:

a. The selected solid pharmaceutical desiccant should have good compatibility with the packaged drug and should not affect drug safety.

b. The sealed packaging of desiccants should be able to block direct contact between desiccants and drugs. At the same time, the materials used for desiccant packaging should have a certain degree of moisture permeability to ensure that the moisture in the packaging system can be absorbed by the desiccant through the packaging layer of the desiccant.

c. The sealed packaging of desiccants should be clearly distinguished from drugs to prevent accidental ingestion as drugs.

d. The sealed packaging of desiccants should have sufficient strength to prevent breakage and contamination of drugs during storage or transportation. The appearance, anti drop, and microbiological limits of desiccant sealed packaging should meet the quality requirements for drug safety. For example, desiccant sealed packaging (such as printing ink on the packaging) should not pose a safety risk to drugs.

5.2 Application of desiccant sealed packaging

Table 2: Types and applications of desiccant sealed packaging

	Sealing packaging materials	Features and Applications		
		Applicable dosage forms	characteristic	application
Silicone desiccant	Bag packaging materials: Non woven fabric (such as high-density polyethylene non-woven fabric). Composite materials (such as polyethylene composite films). paper	Capsules, tablets.	Using the bag making process, the packaging system is filled with desiccant and sealed together with the formulation.	When using non permeable packaging materials, if necessary, the surface of the packaging material should be treated with breathability, such as punching holes. It is necessary to ensure that patients mistakenly take or damage the medication during use.
	Bag, column, tube, can, cylindrical packaging material: HDPE/LDPE/PP/composite material	Capsules, tablets.	/	To ensure the breathability of the desiccant, it is necessary to apply

				breathable treatment on the surface of the packaging material, such as punching holes, if necessary
Molecular sieve desiccant	Same as silicone desiccant	Capsule, tablet, powder liquid double chamber bag solid powder.	Same as silicone desiccant	Same as silicone desiccant
Activated carbon desiccant	Same as silicone desiccant	Capsules, tablets	Same as silicone desiccant	Same as silicone desiccant
Fiber desiccant	Same as silicone desiccant	Capsules, tablets	Same as silicone desiccant	Same as silicone desiccant
	Moisture proof combination cover:	Capsules, tablets, powders.	Integrate the desiccant with the lid to absorb moisture inside	Mixed desiccants such as silica gel and molecular sieve can be

			the packaging and keep the entire environment dry. For pharmaceutical factories, the canning process can be reduced, such as the use of desiccants, which reduces the risk of accidental ingestion for patients.	used.

6. Focus on selecting desiccants for medicinal preparations

When selecting medicinal desiccants for pharmaceutical preparations, it is necessary to use risk management methods based on the characteristics and requirements of the drug. The moisture control requirements of the drug and its packaging system should be thoroughly analyzed and studied for their moisture barrier performance. Based on the management concept of the entire lifecycle of the drug, the corresponding desiccants should be selected. Formulation production enterprises should also control the moisture content of the environment during the production process to ensure that the moisture absorption of the desiccant meets the requirements for moisture control.

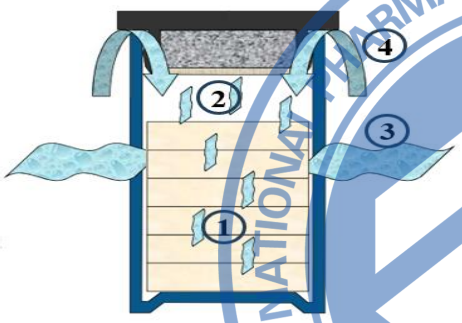
6.1 The pathways of water introduction in pharmaceutical preparations

During the production, transportation, and storage of drugs, the moisture in drugs comes from the following sources:

1. The moisture in the raw materials and excipients of the drug formula itself;
2. The moisture absorbed in the production environment during drug manufacturing and packaging processes;

3. During the storage period of drugs, water in the environment passes through the packaging materials of drugs, such as paper boxes and primary packaging materials, and impact drug quality;
4. For multi dose drug delivery packaging systems, moisture in the environment can enter the initial packaging system after the initial opening of the drug's primary packaging; After the packaging packing is opened, the sealing integrity of the drug packaging system may be affected, which may also cause moisture in the air to enter the drug packaging system. (Figure 2)

Figure 2: Water entry pathways in drug packaging systems



6.2 Focus on drug characteristics and selection of drug desiccants

6.2.1 Selection of Drug Desiccants with Low Moisture Requirements

Ddrugs of humidity sensitivity/low moisture requirements, need to be stored under extremely low humidity conditions. High barrier packaging is usually chosen, and molecular sieve desiccants can be chosen to quickly absorb a small amount of moisture, which can control humidity at an extremely low level. For example, powdered antibiotic drugs in powder-liquid filled into double-chamber bags are extremely sensitive to humidity and easily absorb water during the production process. It is necessary to maintain a dry production environment to ensure that the moisture content of the desiccant is controllable. In addition, during drug storage period, to prevent trace amounts of water from entering the drug through plastic packaging bags; Molecular sieve desiccants can be placed between the primary and secondary packaging in the powder room.

6. 2. 2 Selection of Non Low Moisture Drug Desiccants

Drugs that are not sensitive to moisture do not require extremely low humidity conditions, and generally allow the humidity inside the packaging to be within a certain range (not exceeding 10%). Silicone desiccant can be chosen to absorb the moisture that immigrate into the packaging system during storage, meeting the quality requirements of the drug within its shelf life.

6. 2. 3 Selection of Drug Desiccants with Special Odors

Activated carbon desiccants or mixed desiccants containing activated carbon components can be used in formulations that require adsorption of drug odors (odors), such as metformin tablets.

6. 2. 4 Selection of Drug Desiccants with Multiple Dosages and Multiple Openings

For drugs in multi-dose packaging, after opening, moisture in air from the outside can enter intothe packaging system, potentially affecting the stability of the drugs. During the usage of such drugs, packaging container can be opened multiple times, in order to preventing bagged or barreled desiccants from slipping out of the original packaging system or being discarded by patients, a medicinal moisture-proof combination cover can be selected to continuously control the humidity level inside the packaging system . For example, solid preparations of vitamin effervescent tablets usually use a multi-dose packaging system, and it is advisable to choose molecular sieves or molecular sieve silica gel mixed desiccants to control the humidity level inside the packaging system.

6.3 Key points for storage and use of pharmaceutical desiccants

Desiccants should be stored in sealed and dry containers to prevent moisture increment during storage.

Drug manufacturs should comply with GMP production requirements when loading desiccants into packaging systems during the drug manufacturing process.

During drug manufacturing process, pharmaceutical manufacturs should control the production environment (such as temperature, humidity as necessary, and packaging exposure time in the packaging area) when loading desiccants into the pharmaceutical

packaging system, to avoid desiccants absorbing too much moisture from the environment, which can affecttheir moisture absorption performance.

7 Comprehensive evaluation of desiccants in pharmaceutical applications

7.1 General Provisions

When selecting desiccants and their packaging, it is necessary to consider the entire lifecycle of the drug, based on the concept of risk assessment and the principle of quality by design, and conduct a comprehensive evaluation. The content of comprehensive evaluation should include the performance of medicinal solid desiccants and their impact on drugs, in order to select and use suitable desiccants to ensure the quality and safety of drugs.

7.2 Compatibility study

The selected solid pharmaceutical desiccant should have good compatibility with the packaged drug and should not affect the safety of the drug.

7.3 Stability study

The selected medicinal desiccant should meet the stability requirements of the drug within its shelf life. For multi-dose drugs, it is necessary to simulate the usage scenario of the drug, conduct stability studies on the drug, and ensure that the key quality attributes and safety of the drug are acceptable

7.4 Evaluation of Production System and Quality Management System

Pharmaceutical desiccant production enterprises need to establish corresponding production system and quality management systems.

7.5 Evaluation of product quality characteristics

The quality standard of desiccants should meet the mandatory requirements in Chinese Pharmacopoeia and other agreed requirements in the quality agreement. For example, the appearance, drop resistance, and microbiological limit of desiccants and sealed packaging can be agreed upon and evaluated based on the needs of both parties.

7.6 Meet the adaptability assessment of pharmaceutical production equipment

Meet the product performance requirements for automation pharmaceutical production lines and continuous production, with good appearance performance and minimum defects of desiccant combination covers, stable outer diameter dimensions with

less variation of dimension

7.7 Assessment of the ability to continuously and stably supply products

Having stable supply capacity and supply strategy during urgent situation .