

# **Das Titus-System**

**Ein geschlossenes System für die  
Isolierung von Wirkstoffen**

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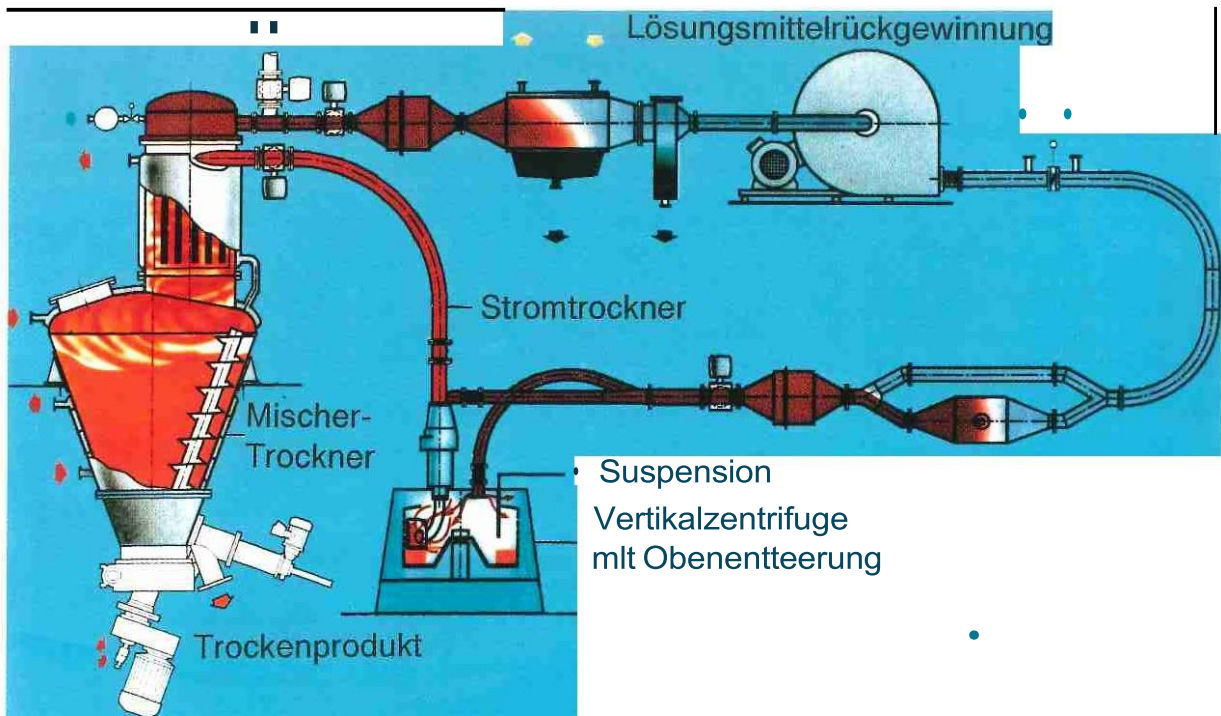


Fig.1. Construction of Titus system

# The Titus system

A closed system for the insulation from Active ingredients

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The Titus system is a process line for automatic product processing from the suspension inlet into the centrifuge to the discharge of the dry product out of dem Dryer. The overall procedure consists out of three stages: separation of the Mother liquor in a vertical centrifuge

.)drainage; separation of the Surface moisture in a flash dryer and separation of the internal moisture in a mixer-dryer.

**The Titus system is a processing line for the automated product processing all the way from entry of the suspension into the centrifuge to discharge of the dry product from the dryer. The overall process comprises three steps: removal of the mother liquor in a vertical centrifuge with top discharge; removal of surface moisture in a flash dryer; and removal of internal moisture in a mixer-dryer.**

Active ingredients fall at of their Manufacturing many times in shape from Solutions at, out of whom they failed or crystallized become. The active ingredients are further isolated using mechanical and thermal separation processes . There are different equipment solutions for implementing the two separation processes , for example a vertical centrifuge with a downstream tumble dryer.

Become the both Separation process in each other separate Apparatus through - guided, so can the following problems appear :

- Contamination of the product due to contamination with foreign particles or with leftovers from the previous batch ; Impairment of the processing properties of the product through broken grain ;
- reduction the durability of the product caused by pathogenic germs;
- Product losses during product transportation;
- Product dust emissions and organic solutions ;
- elaborate product handling;
- long Batch times.

To get around these problems, there are two options:

- Combination of the Separation process in an apparatus, for example Titus - Nutsch - Trock - ner;

- combination the separation process in one closed system e.g. Titus System.

At the combination the Separation process In an *apparatus*, the various process steps (filtration and drying ) take place consecutively (one after the other) .

At the combination the different Separation process in one However , the different *systems* can be used in a *closed system* Process steps simultaneously (temporal + parallel) expire. A prime example of the combination different separation processes in a closed system is this Titu s s y s t e m .

## Construction

The Titus system (Away b. 1) consists in the we essential out of :

- Vertical centrifuge mil top emptying;
- Power dryer mil Solvent pressure recovery and
- Mixer-dryer.

## Vertical centrifuge

The vertical centrifuge consists of a gas-tight Housing with Filtrate drain. The housing is through the Housing cover closed. On dem stable Housing cover are next to the Formwork device

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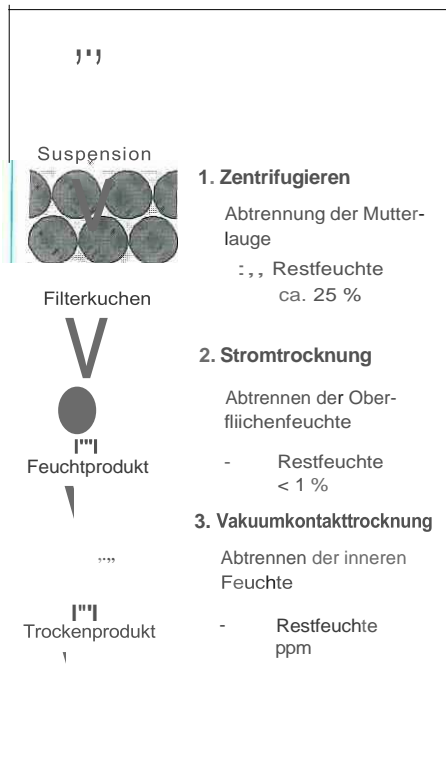


Fig.2. Way of working of Titus system

a Manhole, full pipe, washing pipe and the winding devices are accommodated. The formwork device consisting of a formwork head and a formwork mouth is used for top emptying the vertical centrifuge.

### Power dryer

The connecting line between the vertical centrifuge and the flow dryer is used Cyclone filter of mixer-dryer used. This line is in the rule between 10 and 20 m long. A fan generates the circulating gas volume flow, which allows a pressure increase of up to 350 mbar. In the downstream heating zone the circulating gas is routed to the stream drying section required entry temperature heated up. The temperature becomes through mixture of heating gas streams with a new cold gas flow regulated. This gives itself one very short response time the temperature control, the in the range of seconds lies. The Cyclone filter consists of a cylindrical filter house with a tangential raw gases inlet. As filter elements, filter bags or filter bags can be used. Depending on the requirements, cloths or sintered multi-layer metal fabrics are used as filter media. The filter elements are cleaned using pressure-stroke. If necessary, suspended matter filters or, in special cases, sterile filters can also be used downstream become. The solvent becomes out of the

Circulating gas through a condenser with mist separator condensed out

### Mixer - dryer

in the conical container with a welded heating jacket of the mixer-dryer moisture good submitted and dried. The mixing mechanism is at the outlet of the cone container flanged. It serves for the mixing screw and the rotary drive. Mixing screw and rotating rubber are sealed with low-abrasion lip seals. Mechanical seals are used in sterile operation.

The mixing screw carries out two rotational movements simultaneously in the cone container, and that is one rapid rotation around the mixing screw axis and one slow rotation around the

Cone container axle. The rotation around the cone container axis is drawn according to a full circle (360°). In the opposite direction, so that the supply lines for electricity, heating medium and control air are not twisted. Through the flying storage of the mixing screw means there are no oil-lubricated drive or gear components in the process area.

### Way of working

The Titus system is one process line for automatic product processing (Abb. 2), at of the three procedural steps:

- Separating the Mother liquor through Zen-trifuge;
- Separation of surface moisture through current drying and

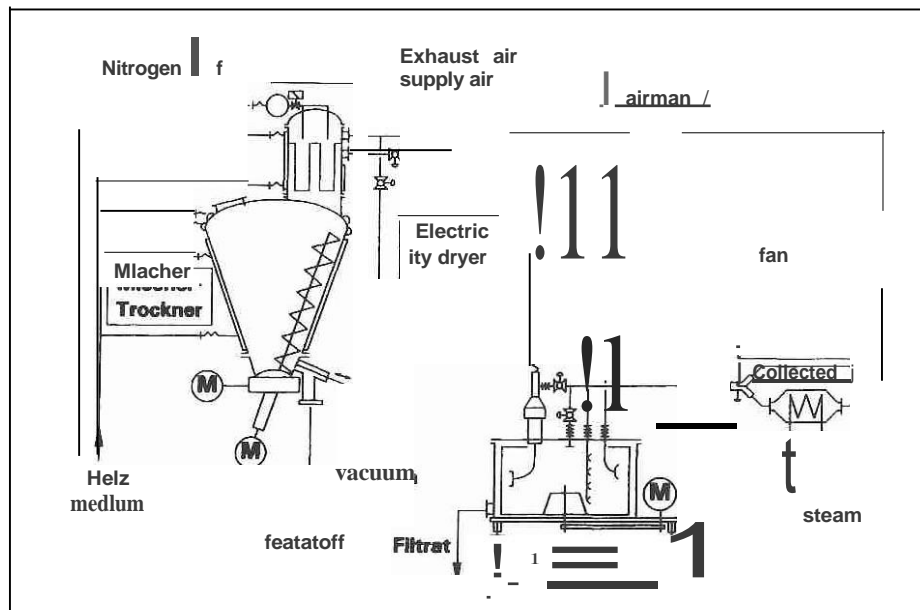


Fig.3. Titus system in more open Execution

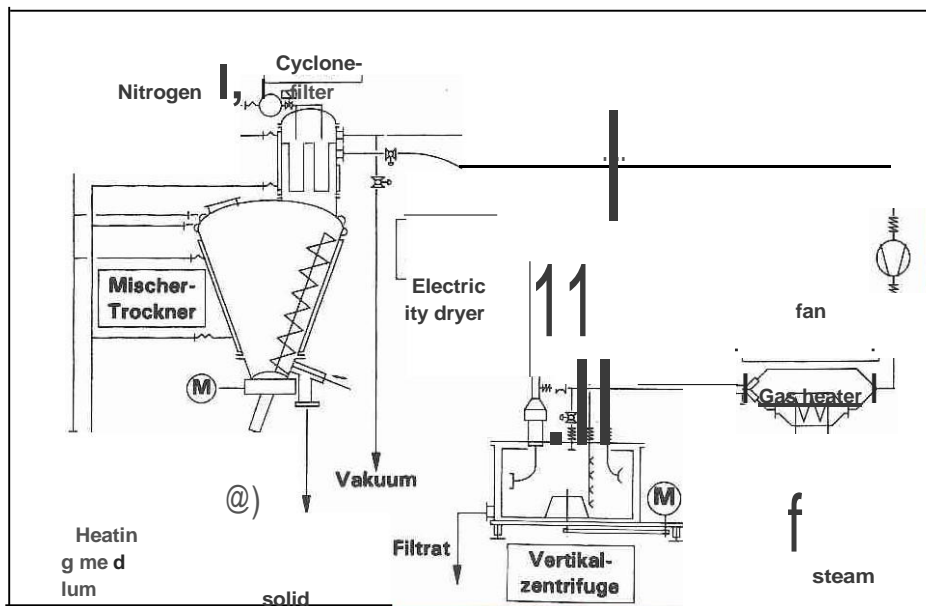


Fig.4. Titus system in more closed Execution

- Split off the internal moisture by vacuum contact drying.

### Centrifuge

In the vertical centrifuge the mother liquor becomes from the product separated, back remains the one centrifuge humidity Filter cake. If

necessary can itself several Wash Connect processes. By drying , a low level of residual moisture is achieved in the filter cake .

### Stream drying

After dem Centrifuge becomes the product with Help the Formwork device out of the Vertical I central joint switched out and with Hi | -

fe of Circulating gas flow pneumatically in the Mixer-dryer required. There for the demand hot cycle gas is used, finds at the same time one convecti-

- Drying takes place , which largely removes surface moisture. At one Scarf speed between 100 and 200 min .<sup>-1</sup> swings the Schalmul in the filter cake and turn the product into chips with a thickness of about 0.5 mm away. The switched off product becomes from the hot cycle gas captured and on approximately 40 m/s accelerated. Through the good Dispersion and the high relative velocities lead to an intense warming and exchange of substances between the moist solid particles and the hot cycle gas. As a result of the low temperatures (cooling limit temperature) and the short residence times (around 1 to 3 s) result in very gentle drying. At the output of the Become a power dryer residual moisture in water-moist products of 0.5 % and at I6 -

leftover products moistened with liquid

- Humidity reaches up to 0.1 % . In the cyclone filter the product from the Gas flow circuit secluded and falls in the of the mixer-dryer below . The circuit gas leaves dryer through the filter elements located inside the cyclone filter - ment, which retains fine particles become.

### Vacuum contact drying

After the cone container is removed by shelling several batches The vertical centrifuge is filled to the desired level Circular gas operation set. A vacuum system puts the closed mixer -dryer under vacuum. At the subsequent one vacuum

contact drying becomes the internal moisture separated. The necessary amount of heat becomes above the heated Cone container and the heated mixing screw are added - lurts. During

mixed. As soon as the required residual moisture reached is, becomes the Vacuum operation completed. Thereafter can the Cone container can be emptied by reversing the mixing screw.

**Table 1. product purity; Number Foreign**

#### particles in 15 G Product.

Foreign particle size6Be particles	number Foreign	Should	is
µm			
50-100		30	5, 70
> 100		4	2.00
fibers		3	0.15

### Operating modes

#### Open system

The Titus system becomes as open System (A b b. 3) applied for air - insensitive Products and unproblematic Moist well (water). Air from the fan is used as the delivery medium the Vicinity sucked in becomes. The

with Steam saturated Exhaust air will discharged into the surrounding area.

#### Closed system , gas-tight

Are the Products sensitive to air and / or loaded with problematic material moisture ( e.g. organic solvents ) . the closed one Titus system (A b b. 4) set on. Nitrogen serves as the transport medium. At this Operating mode becomes the Sy stem before Start of production inerted with nitrogen . Thereafter becomes the Attachment on slightly overpressured to keep acid out of the environment . By monitoring with an oxygen analyzer and readjusting the Nitrogen supply becomes ensured,

thatB the Oxygen content under one before given limit remains.

#### Closed system , pressure-resistant

The Titus system in a pressure-resistant design is for the Processing van sterile, low in foreign particles products applied . Nitrogen is again used as the delivery medium , but at an operating pressure of 2 bar. The pressure-resistant system lets one Steam sterilization up to 133 °C to. A essential Advantage the pressure firm Execution is in this to see thatB

drying the goods become through the Mechanical mixing screw

### Application example

#### Batch expiry (A bb . 5)

#### Pro dI J ct data :

Solid grain size 6Be liquid	Pharmaceutical product - 20 µm isopropanol
Solids content	15 M- %
Suspension rubble weight dry	250 kg/ m <sup>3</sup>

#### Appar ate data

Vertical centrifuge:	VZO 125/2.5
Type drum diameter	1250 mm
drum height filter flat drum content	630mm 2.5 m <sup>2</sup> 400 DM <sup>3</sup>

#### Electric dryer:

Type	TTS 150
Nominal diameter	150 mm
Long Power dryer	20 m

#### Mixer-dryer: type

Heat exchange flat nominal volume	MT 4/300 13 m <sup>2</sup> 4 m <sup>3</sup>
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#### Operating data

##### Centrifuge:

Batch quantity	250 kg atro
Accelerate	200 800 min. <sup>-1</sup> , 4
Fill	800 min. <sup>-1</sup> , 30 min
Wash	800 min. <sup>-1</sup> , 30 min
Accelerate	800 950 min. <sup>-1</sup> , 2 mins
Spin dry	1200 min 1, 80 min
Braking	950 200 min 1, 2 min
batch time f.	
Centrifuge	150 min = 2.5 H

#### Current drying:

Batch quantity	250 kg atro
Circulating gas volume flow	2000 m <sup>3</sup> /H
inlet temp. stream dryer	100 °C
outlet temp. stream dryer	50 °C
outlet temp. product	42 °C
Batch time f.	

Power dryer	30 min= 0.5 H
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#### Vacuum contact drying: (4 centrifuge batches) batch

quantity	1000 kg atro
Pressure	35 mbar
number of revolutions	80 min <sup>-1</sup>
Mixing screw speed	0.3 min. <sup>-1</sup>
rotary drive wall	60 °C
temperature batch time for dryer	12 H

### Product purity

At a constant mass flow the volume flow is lower due to the higher pressure and therefore the Pipe cross sections as well as the filter surfaces of the cyclone filter and the sterile filter can be made smaller (size, costs).

A MaB for the Product purity is the Number of foreign particles in a certain quantity Product. To be 11e 1 there the number of

Foreign particles in 15 g product for ver - different grain classes . At the 1 st - values acts it itself around

average

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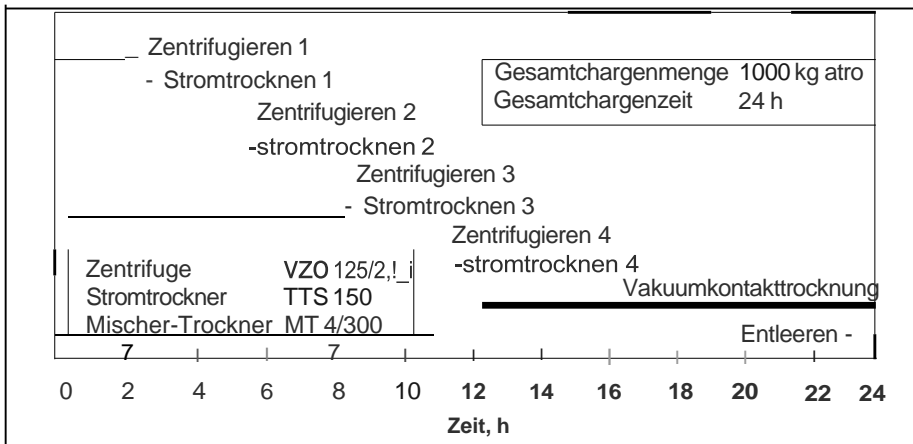


Fig.5 . Batch expiration

values from 20 containers. From the table it can be seen that the  $I_s t$ -values significantly below the specified target values for sterile products lay. The Titus System is therefore ideal for the production of sterile injection ware .

### Grain preservation

Grain preservation is important when isolating active ingredients important. Around she to quantify the grain size distribution during the various processing steps measured. Out of A b b. 6 is ! It can be seen that both the position parameters and the distribution parameters of the grain size distribution hardly change during processing. That 's it! the Grain preservation the processing in Titu s systems has been clearly proven .

### Use areas

The Titus system is primarily used for oiling from solids out of Suspensions used , if following Criteria are met : medium capacities , monoproduction, high product purity , toxic products , solvent-moist products.

The most important areas of application are : - gen in area of Pharmaceutical In industry and fine chemistry .

Ober 200 Products become mi! Success

ver - is working , e.g

- Novocaine - Penicillin ,
- Procaine - Penicillin ,
- tetracycline ,
- Novalgin ,
- streptomycin ,
- Tandaril ,
- vitamin B ,
- Claforan ,
- cephalosporin ,
- acetaminophen ,

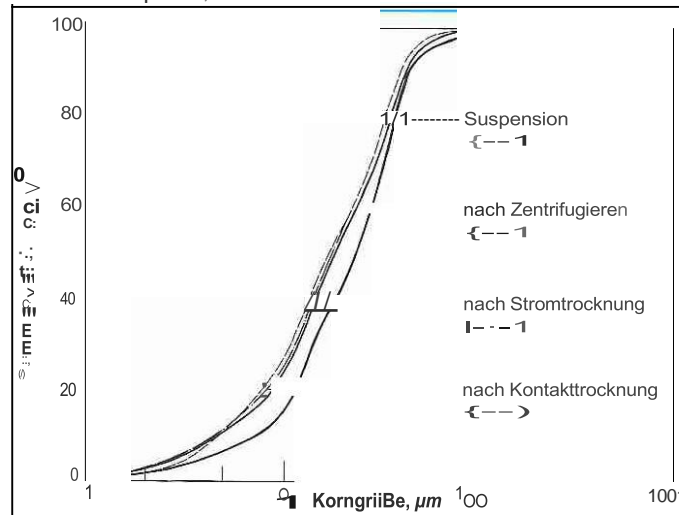


Fig . 6. Grain size distribution during different processing steps in the Titus system

- calcium acetate ,
- guaifenesin ,
- Herbicides.

### Important characteristics of Titus Systems

- Vertical centrifuge mi! automatic top emptying :  
no problems mi! dem product handling ;
- Electric dryer:  
simultaneous Financial support and drying ,  
gentle removal of the  
Upper surface moisture;
- Mixer - Dryer:  
gentle distance the internal humidity ,  
nearly complete emptying;
- Solvent recovery : none  
Ecological damage ;
- Closed system: • Avoidance of  
product losses , avoidance from  
Product contamination ,  
Avoidance from Emissions.

