facts

TCC TB

Tricalcium citrate as excipient for direct compression

Jungbunzlauer

From nature to ingredients®

Introduction

Direct compression has gained enormous popularity in tablet manufacturing in recent times. It is seen as the most economic process in terms of labour, time, equipment, operational energy, and space. What is more, direct compression also has the added advantage of eliminating problems due to heat and moisture that can occur during wet granulation. However, it places great demands on the excipients used in the process. Direct compression therefore requires that tablet formulations (active ingredients and excipients) exhibit good compactibility as well as flowability.

TCC TB is a tricalcium citrate tetrahydrate designed to function as a direct compression excipient. It combines exceptional compression characteristics, good flowability and good tolerability.

TCC TB is produced in a unique production process which creates the special crystalline structure that is responsible for its outstanding characteristics – making it the ideal choice for a direct compression excipient.

Properties of TCC TB

- Tricalcium citrate tetrahydrate with special crystal structure leading to excellent flowability.
- Compacts to tablets of higher tensile strength compared to other brittle fillers.
- Enables production of hard tablets even at low compression forces.
- Retains low relative density even when compressed to hard tablets.
- Shows brittle fracture with plastic deformation and slight elastic relaxation.
- Enables production of tablets with extremely flat surfaces and sharply defined edges.
- Rapid dissolution due to high porosity.
- Can be used for pharmaceutical products as well as for food supplements.
- Calcium in citrate form with excellent tolerability and compatibility.
- Highest purity with very low impurities and very strict microbiological specification.

Manufacturing

TCC TB is produced by complete neutralisation of non-GMO citric acid with a very pure calcium source, which is produced from limestone. TCC TB precipitates from solution to create its special crystalline structure.

Regulatory and quality information

TCC TB is Jungbunzlauer's name for tricalcium citrate tetrahydrate excipient grade and is compliant with the latest versions of the USP and FCC.
TCC TB is very low in elemental impurities and has a very strict microbiological specification.

Table 1: Regulatory information

IUPAC name	2-hydroxy-1,2,3-propane-tricarboxylic acid calcium salt (2:3)
Chemical formula	$Ca_3(C_6H_5O_7)_2 \cdot 4H_2O$
EC No.	212-391-7
CAS No.	5785-44-4
E-No.	E 333

TCC TB is produced in Jungbunzlauer's production facility in Ladenburg, Germany. The facility has been certified according to DIN ISO 9001:2008 and ISO 22000 / PAS 220:2008 and cGMP since 2001. TCC TB is halal (MUI) and kosher certified. Jungbunzlauer continuously invests in sustainability, production standards and efficiency.

General properties of TCC TB

Table 2: General properties of TCC TB (Typical values).

Appearance		**White crystalline granular powder**
Mean particle size (µm)		145
Bulk density (g/ml)	loose tapped	0.56 0.65
Angle of reponse (°)		29
Flowability		Excellent
Water activity		~ 0.2
Solubility (g/l)		1
pH value (2.5% suspension)		~ 5.7

Particle size distribution

TCC TB is a granular powder with a low mean particle size of around 145µm. Figure 1 shows a typical particle size distribution (cumulative distribution and distribution density) of Jungbunzlauer's TCC TB, measured via laser diffraction. The particle size is constantly monitored through in-process-control (IPC) testing and is part of the product specification (table 3).

Figure 1: Typical particle size distribution of TCC TB. CILAS particle size analyser (laser diffraction; wet dispersion).

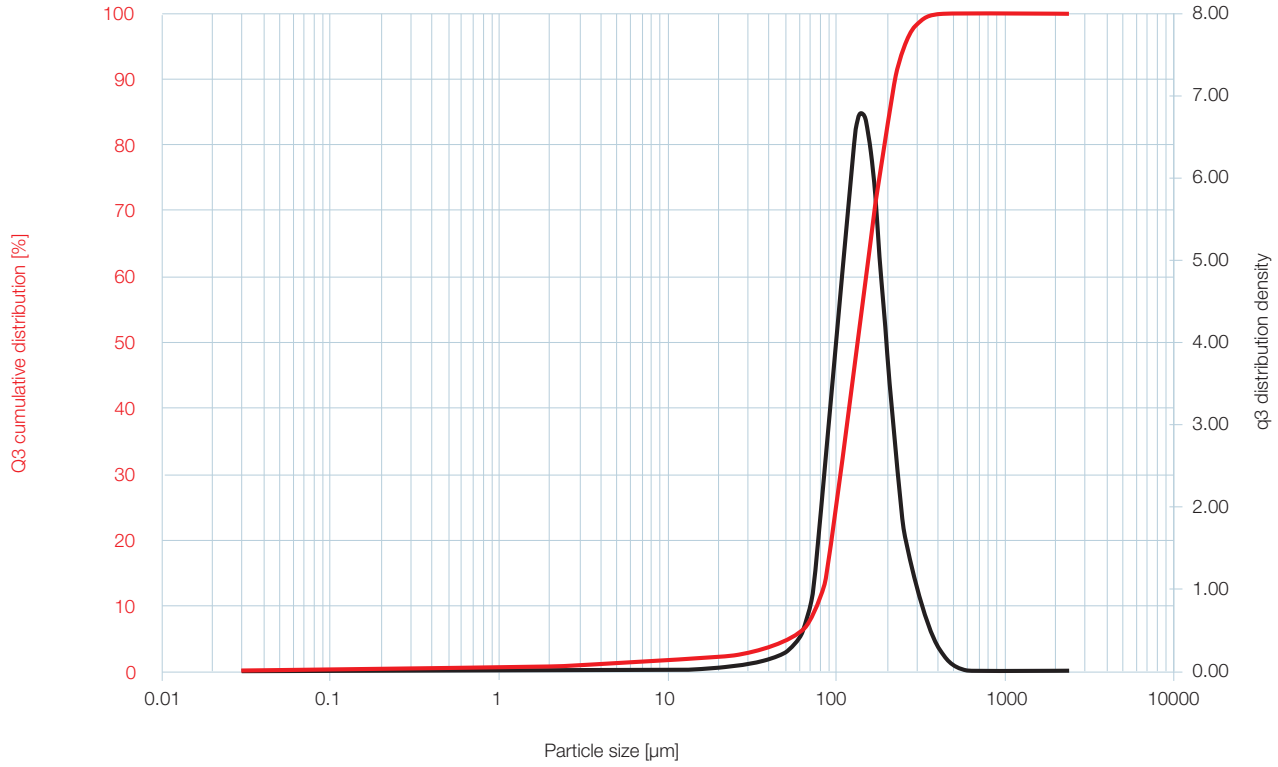


Table 3: TCC TB granulation specification and typical values

Particles		Specified	Typical
<63µm	(NMT)	30%	<10%
<100µm	(NMT)	50%	<25%
<500µm	(NLT)	98%	100%

Flowability

The flowability of powders mainly depends on the particle size distribution as well as on the shape of the particles. Even if TCC TB contains significant amounts of particles smaller than 100µm, it shows excellent flowability, as expressed by the Hausner ratio, compressibility index (Carr's index) as well as its angle of repose (table 4).

Table 4: Flowability characterisation of TCC TB (typical values)

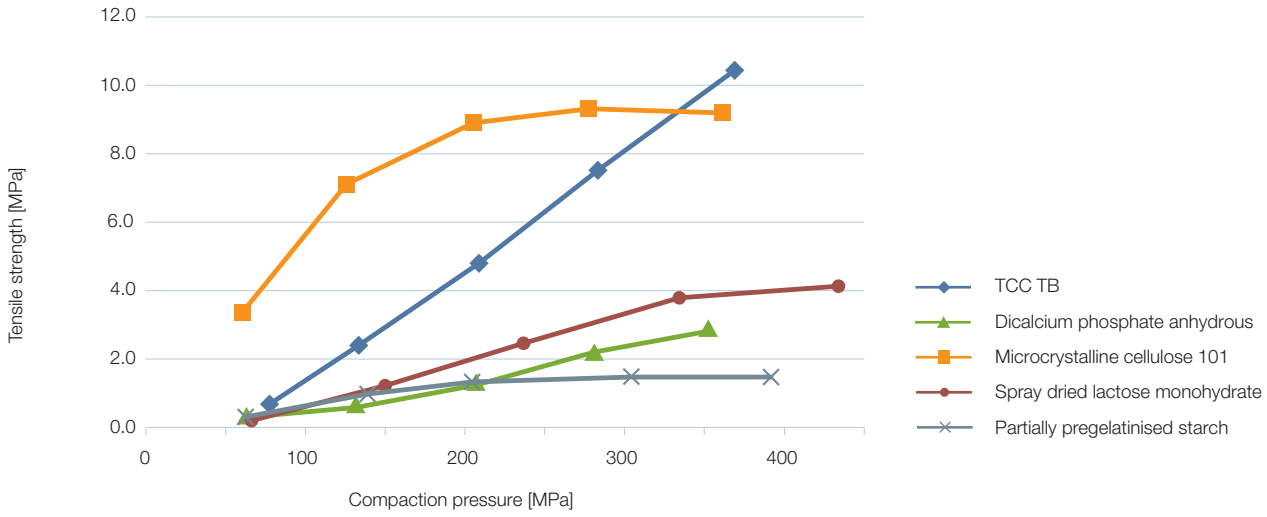
		TCC TB	Thresholds indicating "good flowability"*
Density (g/ml)	bulk tapped	0.56 0.65	n.a.
Hausner ratio		1.16	<1.25
Compressibility index (Carr's index)		13.8	<16
Angle of repose (°)		29	<30

*Patel et al., Critical ReviewsTM in Therapeutic Drug Carrier Systems, 23(1):1–65 (2006)

Compactability

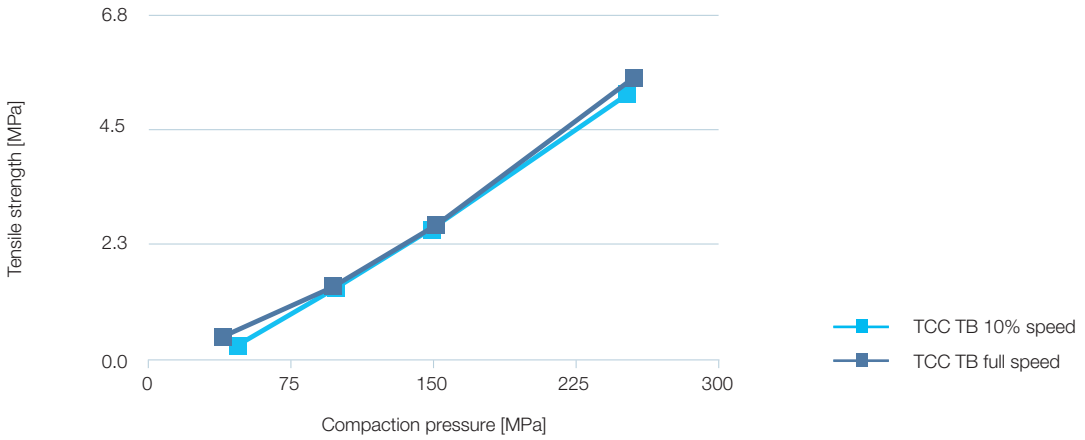
TCC TB is suitable for direct compression. It enables the production of hard tablets, while using reasonable compression forces. Within the range of tested brittle fracture excipients TCC TB stands out in its ability to produce tablets of sufficient tensile strength even at relative low compaction pressures, thus reducing wear on tablet equipment (figure 2).

Figure 2: Compactibility-Plot (Medelpharm StylOne Evolution, 9 mm concave (r=15 mm) miming a Fette 1200 at low speed (17 rpm))[1]



The production of tablets with TCC TB is independent from compression speed. As shown in figure 3, the production of tablets at full compression speed (dark blue line) resulted in similarly hard tablets as when produced at 10% compression speed. This speed in-sensitivity of TCC TB is an important advantage, as it prevents problems from occurring during up-scaling due to increased punch velocity when transferring the product from a station laboratory press to a rotary press.

Figure 3: Compression speed dependency of TCC TB. Compactibility-Plot at full compression speed (900 tablets/h) and at 10% speed (Romaco Kilian StylOne 105 ML; 8 mm flat).

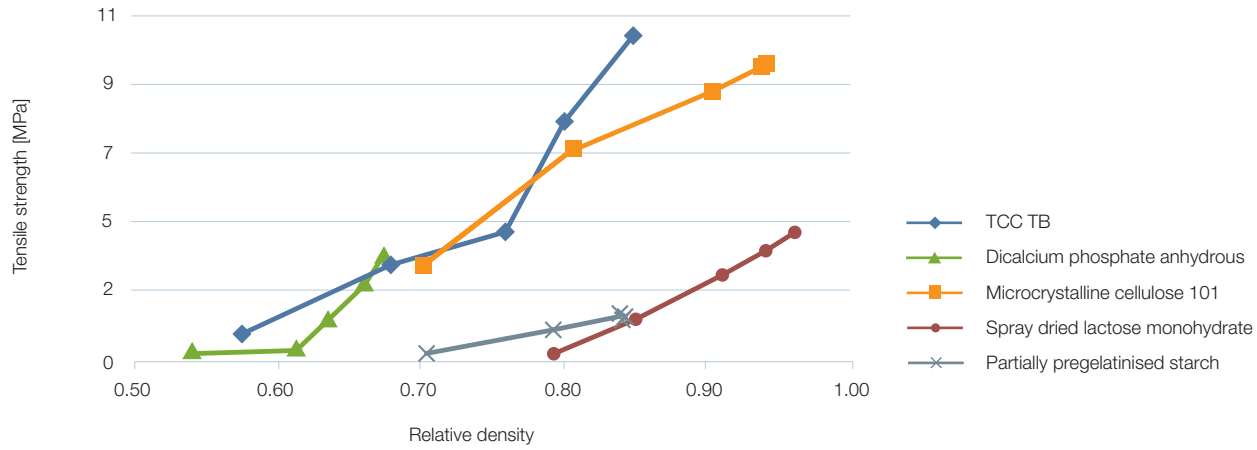


Compression trials on the rotary press (Fette 102i; 9 mm concave) show that the compressibility of TCC TB (+0.5% magnesium stearate) is also independent from the speed of the rotary press (17 RPM vs. 139 RPM), as well as from whether or not pre-compression is used.

Porosity retention

The compression of TCC TB resulted in tablets of high strength at already low compression forces. These tablets tend to retain their low relative density compared to other typically used excipients (figure 4). This higher porosity facilitates the disintegration and dissolution of the tablets.

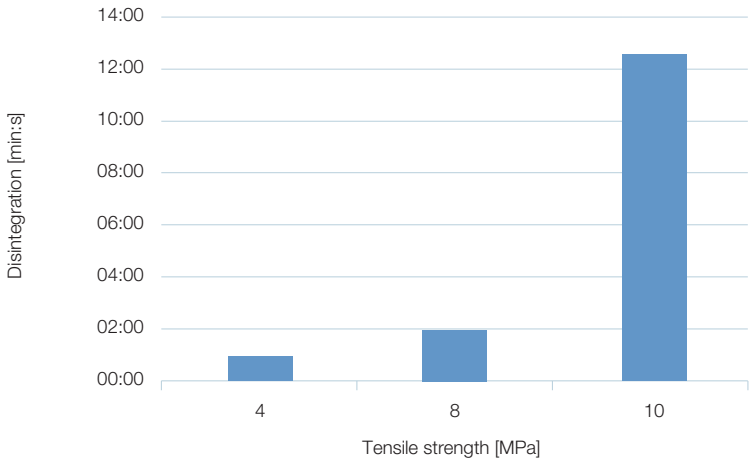
Figure 4: Bondability-Plot (Medelpharm StylOne Evolution, 9 mm concave (r=15 mm) miming a Fette 1200 at low speed (17 rpm))[1]



Disintegration

Tablets produced out of TCC TB easily disintegrate even without the usage of disintegrants. The disintegration time of TCC TB tablets was below 3 min with a tensile strength of up to 8 MPa. These figures were reproducible and independent of results obtained when precompression was applied or not. Figure 5 shows data for tablets produced with precompression only. Note that with a tensile strength of 10 MPa there was an exponential increase in disintegration time.

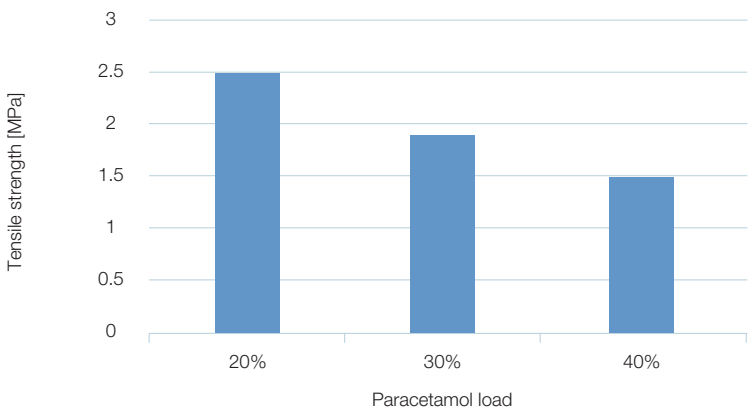
Figure 5: Disintegration time of TCC TB tablets with 0.5% MgSt as internal lubricant (Fette 102i, 9 mm round concave (r = 15 mm); with precompression; 69 rpm (1.01 m/s)).



Loading capacity

The loading capacity of TCC TB is shown in figure 6.
Poor compaction behavior is a known property of fine crystalline paracetamol powder, thus direct compression tableting is hence challenging. Mixtures of TCC TB and fine paracetamol powder at drug loads between 20 and 40 % were compacted on a single punch tablet press. For all drug loads tested, tablets produced with TCC TB showed high tensile strength (>1.5MPa).

Figure 6: Compactibility of mixtures of TCC TB and fine paracetamol powder with 1.0% magnesium stearate as internal lubricant (Romaco Kilian StylOne 105 ML; 8 mm flat; at 25% speed: 225 tablets/h)



Dissolution of these paracetamol tablets was very fast (Apparatus 2 (paddle), 75 rpm, medium: 900 ml 0.1 N HCl, 37 ± 0.5 °C.). All formulations (20%, 30% and 40% paracetamol load) released more than 83% paracetamol after 2 min.

Compression behaviour

During compression, TCC TB undergoes a rearrangement phase at the beginning. Afterwards the particles show brittle fracture with plastic and only slight elastic deformation (figure 7). Compared to other brittle substances, like dicalcium phosphate anhydrous or spray dried lactose, the elastic relaxation of TCC TB is slightly more pronounced (table 5).

Figure 7: Heckel-Plots of TCC TB (Romaco Kilian StylOne 105 ML; 8 mm flat; 10% speed: 90 tablets/h)[1]

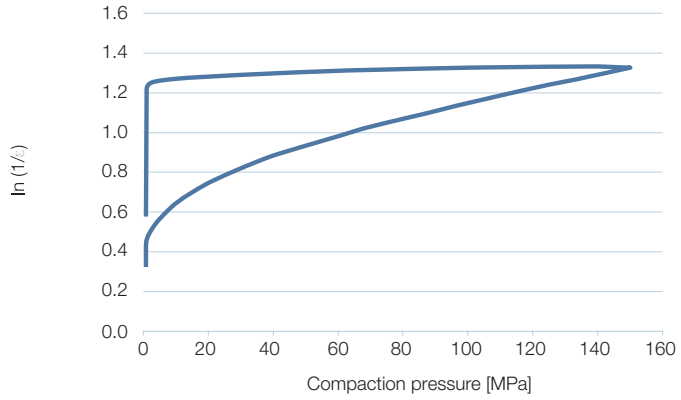


Table 5: Elastic Relaxation, in- & out-of-die method 24h

	Elastic relaxation
TCC TB	7.2%
Spray dried lactose monohydrate	6.3%
Dicalcium phosphate anhydrous	5.1%
Partially pregelatinised starch	24.8%
Microcrystalline cellulose 101	13.9%

With its relatively low elastic relaxation, TCC TB enables a subsequent coating step without a long lasting rest period for post-compaction viscoelastic strain recovery. At the same time, it also retains sufficient relaxation to avoid tablet defects when combining it with other elastic tablet constituents.

Reference

[1] Veronika Hagelstein, Markus Gerhart & Karl G. Wagner (2018): Tricalcium citrate – a new brittle tableting excipient for direct compression and dry granulation with enormous hardness yield, Drug Development and Industrial Pharmacy.

About Jungbunzlauer

Jungbunzlauer is one of the world's leading producers of biodegradable ingredients of natural origin. We enable our customers to manufacture healthier, safer, tastier and more sustainable products. Due to continuous investments, state-of-the-art manufacturing processes and comprehensive quality management, we are able to assure outstanding product quality. Our mission “From nature to ingredients®” commits us to the protection of people and their environment.

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