BASF
We create chemistry

Kollitab™ DC 87 L

Your all-in-one tableting solution

Coprocessed excipients are a combination of two or more materials without undergoing any chemical changes. These excipients are increasingly being recognized as a viable solution to address the challenges associated with active pharmaceutical ingredients (APIs) in direct compression applications.

Figure 1.
Kollitab™ DC 87 L composition

Figure 2. Free-flowing Kollitab™ DC 87 L

The primary objective in developing a coprocessed excipient is to enhance its material properties by integrating key functionalities such as filler, binder, disintegrant, and lubricant into a single material. This approach not only improves the processability of the drug but also guarantees superior performance of the final product.

Kollitab™ DC 87 L (Kollitab™) is an all-in-one coprocessed excipient designed for direct compression of solid oral dosage forms. It was strategically designed to encompass all basic functionalities required for tablet manufacturing: lactose monohydrate as filler, fine crospovidone (Kollidon® CL-F) as the disintegrant, PEG-PVA grafted (Kollicoat® IR) as the binder, and sodium stearyl fumarate (SSF) as the lubricant (Figure 1). Kollitab™ offers excellent flowability, as depicted in Figure 2, ensuring good blending properties and low mass variation during the manufacturing process. Additionally, it exhibits excellent tabletability, enabling easy and efficient tablet compression. Moreover, tablets formulated with Kollitab™ present fast disintegration times, allowing for rapid drug release and absorption.

As a result, Kollitab™ fulfills the primary requirements for tableting, thereby reducing the number of ingredients needed in the formulation. This simplifies the development process and consolidates Quality by Design (QbD) efforts. It also minimizes testing expenses by reducing quality control analysis, as well as material handling and documentation.

Simplifying formulations with two single ingredients: API + Kollitab™ DC 87 L

Kollitab™ DC 87 L is a versatile “all-in-one” coprocessed excipient designed for direct compression formulations. Its exceptional processability and performance simplify the manufacturing process by enabling a single dry blend with the active pharmaceutical ingredient (API) using standard process equipment. In instances where highly cohesive and micronized drugs are utilized at a high formulation load, additional lubricant concentrations may be necessary. Additionally, stabilizers or solubility enhancers, such as antioxidants and poloxamers, can also be included in the drug product to overcome any drug-related challenges. Once for all, formulation optimization can be reached faster if Kollitab™ is used in initial feasibility trials.

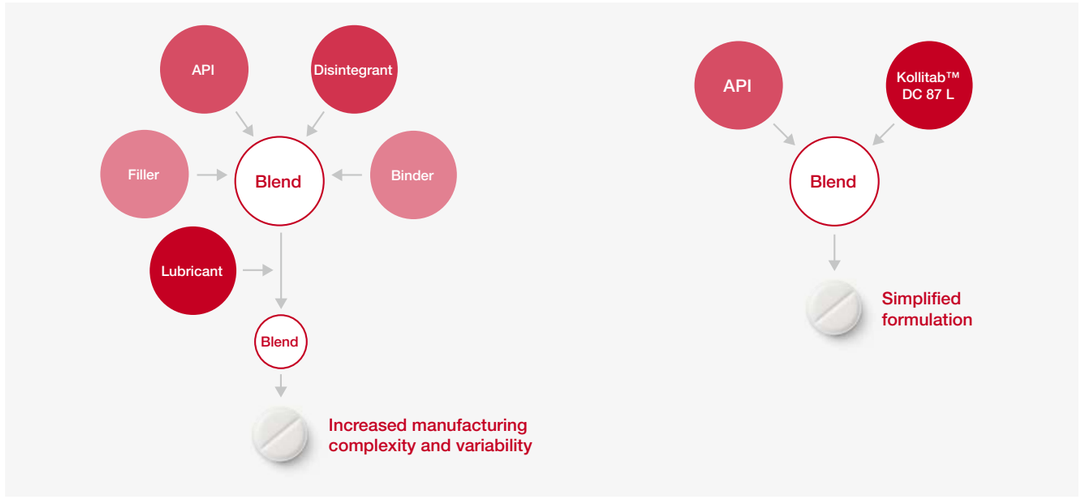


Figure 3. Simplified feeding process with Kollitab™ DC 87 L compared to the complex multiple dispensing of several ingredients

Streamline continuous manufacturing with Kollitab™

Direct compression continuous manufacturing (DCCM) is becoming more popular in the pharmaceutical industry due to its many advantages and Kollitab™ has emerged as a valuable tool to enhance this process. The simplified formulation of typically two ingredients, the drug and Kollitab™, enables faster material characterization and shorter design of experiments (DOE). This results in significant time and cost savings during the development process. The reduced number of loss-in-weight (LIW) feeders, as presented in Figure 3, streamlines control strategies and reduces overall complexity. Kollitab™ also simplifies modeling development and process analytical technology (PAT), enhancing the accuracy of predictions and improving process control. Lastly, Kollitab™’s flow properties not only help reduce noise and disturbances during the feeding process but also enhance the blending process, resulting in improved drug uniformity.

Case studies

Below are two case studies that highlight how the use of this all-in-one coprocessed excipient can accelerate development and expedite time-to-market.

Lamivudine 150 mg

Lamivudine is a pyrimidine nucleoside analogue that is prescribed for the treatment of HIV infection in both adults and children. It is typically used as part of a combination therapy with other antiretroviral drugs. This drug is available as a white to off-white crystalline solid, which has a moderate solubility in water at 20°C and melting point range of 170-175°C. Lamivudine has a very poor flow and is typically not suitable for a direct compression (DC) process using ordinary excipients. In order to simplify and streamline the development process for an immediate-release lamivudine tablet, the potential of using Kollitab™ was explored, targeting a high drug load formulation through DC.

Lamivudine formulation and tableting specifications can be found in Table 1, while the particle characteristics of both API and Kollitab™ and their blend are listed in Table 2.

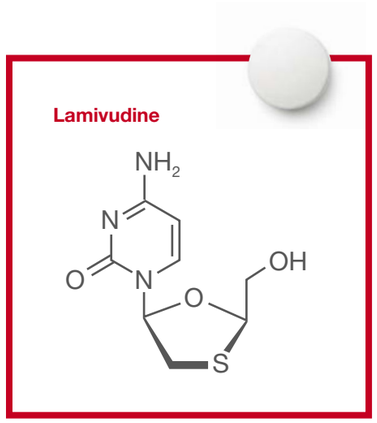
Table 1. Formulation of lamivudine 150 mg with Kollitab™

Formulation lamivudine 150 mg	
Lamivudine	40.00 %
Kollitab™ DC 87 L	60.00 %
Tablet mass	375 mg
Carr index (blend)	14.5 %
Hausner ratio (blend)	1.12

Tableting	
Technology	Rotary tablet press
Equipment	Karanavati (8 stations)
Punch	9.0 mm
Shape	Round flat
Hardness target	90 – 160N

Table 2. Kollitab™ DC 87 L and lamivudine properties

Parameter	Kollitab™ DC 87 L	Lamivudine	Blend Kollitab™ and lamivudine
Bulk density [g/mL]	0.56	0.26	0.53
Tapped density [g/mL]	0.61	0.39	0.62
Hausner ratio	1.09	1.50	1.17
Carr index (%)	8.2	40.0	14.5
Particle size (Malvern):			
d10 [µm]	76	6	
d50 [µm]	158	35	
d90 [µm]	275	97	



The manufacturing process involved sifting lamivudine with Kollitab™ through a 40-mesh screen twice before loading them into a double cone blender and then, mixing for 13 minutes at 24 rpm. After blending, the material was discharged and compressed. Kollitab™ and lamivudine mixture exhibited good flow properties and compressibility during the compression stage, indicating the suitability of a streamlined DC process with only two components.

Table 3 presents the results of both accelerated and long-term stability studies conducted over a period of six months (6M). As indicated, no differences were observed between the initial and final time points. Furthermore, the results for drug impurities were found to be below the limits, confirming the formulation's stability.

Table 3. Initial and 6M stability results of lamivudine 150 mg formulated with Kollitab™

Test	Initial	6M - 25°C / 60 % RH	6M - 40°C / 75 % RH
Appearance	White to off-white tablets	Complies with initial	Complies with initial
Weight (mg)	378 – 381	382 – 385	377 – 382
Hardness (N)	140 – 155	150 – 160	145 – 165
Thickness (mm)	5.20 – 5.30	5.22 – 5.29	5.23 – 5.30
Diameter (mm)	9.03 ± 0.2	9.02 ± 0.04	9.04 ± 0.2
Disintegration (sec)	120	150	135
Assay (%) (90-110)	100.2	102.3	102.6
Related substances			
Cytosine (NMRT 0.2 %)	ND	ND	ND
Lamivudine-S-Sulfoxide (NMRT 0.2 %)	ND	ND	ND
Lamivudine-R-Sulfoxide (NMRT 0.2 %)	ND	ND	ND
Any other impurity (NMRT 0.2 %)	0.010	0.01	0.034
Total impurities (NMT 2.0 %)	0.010	0.014	0.15

Dissolution studies were conducted on the initial and 6M stability samples, following these conditions: apparatus II at 50 RPM, water, 900 mL, 37.5° C; the results are presented in Table 4. In both cases, a dissolution above 85 % within 15 minutes was observed for all samples.

Table 4. Initial and 6M stability dissolution test results of lamivudine 150 mg tablets formulated with Kollitab™

Time (min)	Limit	Initial	25 °C / 60 % RH	40 °C / 75 % RH
5		74	95	94.1
10		99	98	93.1
15	NA	105	99	97.7
20		105	99	96.6
30		105	104	100.2
60	NLT 80 %	105	103	100.1

High-lamivudine-load tablets presented fast dissolution and excellent stability results during the accelerated test period of 6 months. Furthermore, the blend of Kollitab™ and the drug displayed favorable flow properties, ensuring a robust and uniform tableting process. This was crucial for achieving consistent tablet quality and minimizing variations in drug content.

Levocetirizine 5 mg

Levocetirizine dihydrochloride (levocetirizine) is an FDA-approved antihistamine medication that is used to treat various allergic conditions. It is a white to off-white powder with poor flow. It is a BCS class I drug and freely soluble in water, having a higher melting point of 220 – 225°C.

Following the formulation described in Table 5, the micronized levocetirizine was sifted through a 40-mesh screen twice, then loaded into a double cone blender. The API was blended with Kollitab™ for 13 minutes at 24 rpm. Upon completion of the blending process, the material was discharged and compressed. As shown in Table 6, the tableting process resulted in a target hardness, low tablet mass variation, friability, and disintegration time. Additionally, no issues of punch sticking were reported.

Table 6. Initial and 1M stability results levocetirizine 5 mg formulated with Kollitab™

Test	Initial	1M – 25°C / 60 % RH	1M – 40°C / 75 % RH
Weight (mg)	101 ± 2	102	101
Hardness (N)	71 – 90	75	78
Thickness (mm)	3.20 – 3.21	3.20	3.21
Diameter (mm)	6.02 ± 0.2	6.02	6.00
Disintegration (sec)	165	150	135
Friability (%)	0.3 %	ND	ND
Assay (%)	**101.2**	**100.5**	**101.0**

Levocetirizine dihydrochloride

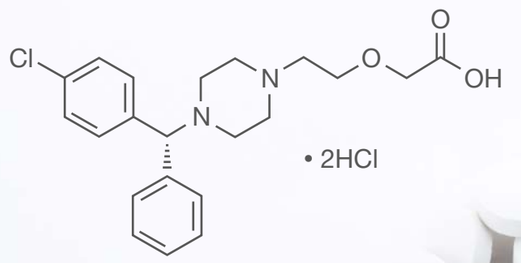


Table 5. Formulation of levocetirizine 5 mg with Kollitab™

Formulation levocetirizine 5 mg	
Levocetirizine dihydrochloride	5.00 %
Kollitab™ DC 87 L	95.00 %
Tablet mass	**100 mg**

Levocetirizine dihydrochloride	
PSD	
d(10)	0.64 µm
d(50)	4.92 µm
d(90)	16.54 µm
Specific surface area	3574 m²/kg

Tableting	
Technology	Rotary tablet press
Equipment	Karanavati (8 station)
Punch	6.0 mm
Shape	Round concave
Hardness target	60 – 100 N

Stability studies were conducted for one month (1M) and no differences from the initial time points were observed.

Five pooled samples sets were created containing 10 tablets each. The tablets were individually assayed, and the average and % RSD results are reported in Table 7. Mean assay and % RSD were within the acceptable limits.

Dissolution studies were carried out following these dissolution conditions: apparatus II at 50 RPM, water, 900 mL, 37.5 °C, for initial and one month (1M) stability samples, as presented in Figure 4. For all, a fast dissolution was observed.

In conclusion, the use of Kollitab™ DC 87 L in drug product formulations offers a range of advantages. These include the elimination of the need to source and test multiple excipients, resulting in reduced efforts in formulation DOEs. Furthermore, this streamlined approach leads to improved efficiency in the overall process, contributing to time and cost reductions, all while achieving optimal drug product performance and quality.

Table 7. Content uniformity of levocetirizine 5 mg tablets formulated with Kollitab™

Sampling	Mean assay % (Limit 90 – 110 %)	% RSD (RSD < 5 %)
Set 1	104.8	3.2
Set 2	102.5	1.8
Set 3	95.8	1.2
Set 4	96.1	0.7
Set 5	101.9	1.1
Assay	**98.6**	**0.8**

Levocetrizine dissolution study-1M stability

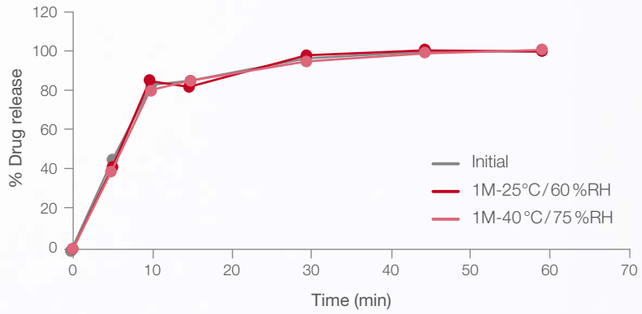


Figure 4. Initial and 1M stability dissolution test results of levocetirizine 5 mg tablets formulated with Kollitab™

Product information	Kollitab™ DC 87 L
Composition	■ Lactose monohydrate ■ Kollicoat® IR ■ Crospovidone ■ Sodium stearyl fumarate
Quality and regulatory information	Full information available on BASF WorldAccount and RegXcellence®. Regulatory Information File (RIF) is available on request.
US DMF Type IV number	038641
Packaging	20 kg cardboard box with PE liner 600 kg per pallet
Article number	50708787

BASF

We create chemistry

Access to standard quality and regulatory documentation is now more efficient than ever. Retrieve your documents 24/7. Sign-up for RegXcellence®, your free online Quality & Regulatory Assistant that provides a unified platform for compliance documents, filing assistance and audit information.

Sign-up today at:
virtualpharmaassistants.basf.com

For more information about Kollitab™ DC 87 L
pharma.basf.com/products/kollitab-dc-87-l

For sample requests contact us at
pharma.basf.com/request-a-sample?product=kollitab-dc-87-l

Speak with an expert
pharma.basf.com/speak-with-an-expert