Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(3), 1963-1970 | ISSN:2251-6727

Process Validation of Ursodeoxycholic Acid Tablet Ip 300 Mg.

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(Received: 16 March 2025 Revised: 20 April 2025 Accepted: 12 June 2025)

KEYWORDS

Process validation, Ursodeoxycholic acid Tablets, Quality assurance, cGMP, Wet granulation

ABSTRACT:

Introduction: Process validation is a critical aspect of current Good Manufacturing Practices (cGMP) ensuring consistent production of pharmaceutical products meeting predetermined quality criteria. This study presents the prospective process validation of Ursodeoxycholic Acid (UDCA) Tablets 300 mg using three consecutive commercial-scale batches. The manufacturing process involved wet granulation, compression, and film coating, and was evaluated for critical process parameters (CPPs) and critical quality attributes (CQAs).All three batches conformed to quality specifications, confirming process consistency and robustness. This paper emphasizes the importance of a structured validation approach in guaranteeing product quality, safety, and efficacy.

Objectives: . The primary objective of validation is to ensure consistent product quality throughout the entire production lifecycle. It serves as a vital component of quality management systems, guiding manufacturers to meet regulatory expectations related to process validation.

Methods: All analytical methods (assay, dissolution, impurities) were validated according to ICH Q2 (R1). Standards traceable to Pharmacopeial reference materials were used. Data were recorded in Validation Batch Records and compared to predetermined targets.

Results: The samples were collected and tested as per sampling protocols .The observations made during each critical step which are discussed in our research work which are given in detail.

Conclusions: The manufacturing process for Ursodeoxycholic Acid Tablets 300 mg was successfully validated using a prospective approach. . All three validation batches consistently met the predefined critical quality attributes (CQAs) and regulatory specifications, confirming the process is robust, reproducible, and suitable for routine commercial manufacturing.

- **Introduction**

In the pharmaceutical industry, validation is a fundamental requirement under Current Good Manufacturing Practices (cGMP) . It plays a crucial role in both internal control and overall quality assurance. Regulatory authorities place significant emphasis on validating every process involved in drug manufacturing . The primary objective of validation is to ensure consistent product quality throughout the entire production lifecycle. It serves as a vital component of quality management systems, guiding manufacturers to meet regulatory expectations related to process validation.

European commission definition for Validation as follows :

Process validation provides documented evidence that a manufacturing process consistently operates within defined parameters to produce a pharmaceutical product that meets predetermined quality attributes and specifications. It is a formal, systematic approach that demonstrates the method's suitability to deliver reliable and consistent results for its intended purpose.

Analytical methods, which are essential for performing accurate analysis, form a core component of the pharmaceutical quality system. The Quality System (QS) regulation defines process validation as the establishment—through objective evidence—that a

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process consistently yields a product that meets its specified requirements. According to section 820.75 of the QS regulation], validation is crucial in ensuring that manufacturing processes are capable of consistently producing products suitable for their intended use. This requirement applies broadly to both drug and medical device manufacturing, emphasizing that quality must be built into every step of the production process. .

The primary objective of any pharmaceutical manufacturing facility is to produce products that meet the required quality standards at the lowest feasible cost. To achieve this, **Good Manufacturing Practices (GMP)** mandate that all critical processes affecting product quality must be validated. The underlying rationale is straightforward: investing in robust development and validation at the early stages of production significantly reduces the risk of failures throughout the product's lifecycle.

The main objectives of **process validation** are:

- To demonstrate that the process consistently performs as intended.
- To confirm that the process is under control.
- To identify and establish acceptable limits for critical process variables.
- To implement appropriate in-process controls.

By validating processes, manufacturers can ensure that each evaluated step reliably delivers the expected results. Successful validation efforts contribute to building quality into the manufacturing process itself, reducing the dependency on end-product testing.

Processes are developed in accordance with **design controls** and then validated. The **process specifications**—also referred to as parameters—are derived from the specifications of the product, component, or entity to be produced. These parameters are documented in the **Device Master Record**.

In pharmaceutical manufacturing, **Quality Assurance (QA)** and **Validation** work in tandem, functioning like two wheels of a chariot, ensuring that product quality is consistently maintained [10]. Processes are developed with the aim of reliably achieving the defined parameters.

Given the complexity and diversity of procedures and activities that require validation, the field is typically divided into several key subsections, including (but not limited to):

- Process Validation
- Cleaning Validation
- Analytical Method Validation
- Equipment Qualification
- Computer System Validation

"Process validation is establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality characteristics."

Process validation is the key element to ensure the identity, purity, safety, and efficacy of drug products. Depending on the complexity of the manufacturing process, several equipments, process and product parameters are optimized at a smaller scale compared to the production size batch. Once the formulation composition and manufacturing process are optimized at the smaller scale, the next stage involves optimizing the process at a larger scale, usually using production equipment by technology transfer group. Increases in batch size or scale-up are accomplished by using larger, high speed equipment that may require adjustments to the process parameters established using small scale equipment.

The strategy selected for process validation should be simple and straightforward. The following factors are considered during prospective process validation:

1. The use of different lots of components should be included, i.e., APIs and major excipients.
2. Batches should be run in succession and on different days and shifts.

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3. Batches should be manufactured in equipment and facilities designated for eventual commercial production.

4. Critical process variables should be set within their operating ranges and should not exceed their upper and lower control limits during process operation. Output responses should be well within product finish specifications.

5. Failure to meet the requirement of the validation protocol with respect to process input and output control should be subjected to requalification following a thorough analysis of process data and formal review by the CMC coordination committee.

- **Objectives**
- To carry out the validation studies of the prepared Ursodeoxycholic Acid Tablet in order to develop a process validation approach as a quality assurance means.
- To carry out process validation studies for the three batches formulated.
- Batch A
- Batch B
- Batch C

- To decrease dissimilarity between different batches, by ensuring the consistency in the manufacturing operations and process.

- To maintain the quality of the prepared product.

- The scope of this project is to minimize the errors in the process validation.

- To find out the uniformity in the batches.

- To perform the in-process monitoring of critical manufacturing stages and end product testing in case of fully validated procedure.

- To maintain the process validation control variables such as the analytical procedure, equipment, production process.

- To find out the results that are obtained is within the acceptance criteria.

- **Material and Methods**

The following section briefly explains materials (formula), equipments and standard manufacturing process used for production ofUrsodeoxycholic Acid Tablet 300 mg IP. Further the manufacturing process of Ursodeoxycholic Acid Tablet 300 mg IP was validated as per master formula record.

The manufacturing formula consists of various excipients each specific in their function used for smoothing the process. Without excipients most drug and pharmaceutical ingredients cannot be compressed in to tablets. This is primarily due to the poor flow and cohesive properties of most drugs.

They may include various diluents, binders, disintegrants, lubricants, glidants and colorants.

Details of raw material specification

S.No.	INGREDIENTS	SPECIFICATION
DRY MIX		
1.	Ursodeoxycholic Acid	IP
2.	Microcrystalline Cellulose	IP
3.	Sodium Lauryl Sulphate	IP
4.	Maize Starch	IP
5.	Croscarmellose Sodium	IP
BINDER SOLUTION		
1.	Polyvinylpyrrolidone	IP
2.	Purified water	qs
LUBRACATION		
1.	Sodium starch glycolate	IP
2.	Magnesium Sterate	IP

1. **Blending:** UDCA API and all dry excipients (except lubricant) were loaded into a V shell blender and mixed for 10 minutes. Homogeneity was ensured before wetting.

2. **Wet Granulation:** A binder solution (5% w/v Povidone K-30 in purified water) was sprayed into the mixer. A high shear granulator (e.g. Diosna or

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equivalent) operating at 300 rpm impeller speed and 50°C was used. Binder spray rate (e.g. 200 ml/min) and mixing time were controlled to achieve a wet mass with target moisture ~3%. In-process checks (e.g. granule "snowball" test) verified endpoint.

3. **Drying:** Wet granules were transferred to a fluid-bed dryer (Glatt GPCG-1). Drying continued until granule moisture content was ≤2.0% (measured by Loss on Drying). Drying temperature (≤60°C) and time were recorded.

4. **Sizing:** The dried granules were milled through a 20#mesh screen to break agglomerates, ensuring uniform granule size.

5. **Lubrication:** Magnesium stearate (1% w/w) was added, and the mixture was blended in a double-cone blender for 3 minutes to uniformly coat granules.

6. **Compression:** Lubricated granules were fed to a 10-station rotary tablet press (Cadmach model or similar) fitted with 10 mm round bevel-edge punches. Compression settings (fill depth, turret speed ~15 rpm, upper punch pressure ~20 kN) were set to achieve tablets of ~310 mg weight containing 300 mg UDCA. Target hardness was ~80 N. Tablet dimensions and weight were recorded during compression (first 100 tablets, then every 5,000 tablets).

7. **Coating (if applicable):** Tablets were film-coated in a coating pan with a solution of HPMC/talc/TiO2 (typical Opadry® formula) to improve appearance and swallowability. Coating parameters (inlet air temp ~55°C, spray rate, pan speed) were controlled per SOP.

8. **Packaging:** Coated tablets were inspected and packed in aluminium-PVC blisters (10×10) under controlled humidity.

Sampling and Analysis: Samples were collected for each stage: blend samples after dry mixing (for uniformity), granules post-drying, and finished tablets after coating. For each batch, the following tests were performed:

- **Blend Uniformity:** Three sub-samples from the blended granules were assayed by HPLC to determine % API; relative standard deviation (RSD) ≤5% was the acceptance criteria.
- **Assay and Content Uniformity:** Final tablets (10 units per batch) were tested for UDCA content by a validated HPLC method. Acceptance was 100±2% label claim (internal spec) with RSD ≤2%. For content uniformity (ICM), USP <905> criteria (individual 85–115%) were checked.
- **Weight Variation:** Twenty tablets were individually weighed. For a target mass ~310 mg (300 mg API), ±5% tolerance is acceptable (none outside ±10%).
- **Tablet Hardness and Friability:** Hardness was measured (n≥10) using a tablet hardness tester; target ~80 N. Friability (n=20) was tested (USP <1216>) and should be ≤1%.
- **Disintegration:** One tablet from each batch was tested (USP <701>); target <30 min in water at 37°C.
- **Dissolution:** Conducted in USP Apparatus II (paddle) at 100 rpm, 900 mL phosphate buffer pH 8.0 (40°C) Samples were withdrawn at 15, 30, 45 minutes. The acceptance threshold was Q ≥85% dissolved by 45 minutes.
- **Microbial Limits:** Total aerobic microbial count (TAMC) and yeast/mold count (TYMC) were determined per USP <61>/<62>. The acceptance per in-house policy: TAMC ≤1000 CFU/g, TYMC ≤100 CFU/g; no objectionable organisms (E. coli, Salmonella, S. aureus) detected.

All analytical methods (assay, dissolution, impurities) were validated according to ICH Q2(R1). Standards traceable to Pharmacopoeial reference materials were used. Data were recorded in Validation Batch Records and compared to predetermined targets.

- **Results**

Parameters	Acceptance Criteria	OBSERVED RESULT		
		Batch-A	Batch - B	Batch-C

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Parameters	Acceptance Criteria	OBSERVED RESULT		
		Batch-A	Batch - B	Batch-C
Description	White to off white coloured, elongated, biconvex, uncoated tablets, having scored on one side and plain on other side.	Complies	Complies	Complies
Identification				
By IR	To comply	Complies	Complies	Complies
By HPLC	In the assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.	Complies	Complies	Complies

Length	15.80 to 16.20 mm	Min.	15.89 mm	15.98 mm	15.93 mm
		Max.	16.06 mm	16.05 mm	16.03 mm
Width	7.80 to 8.20 mm	Min.	7.98 mm	7.97 mm	7.98 mm
		Max.	8.08 mm	8.03 mm	8.04 mm
Thickness	5.40 to 5.80 mm	Min.	5.52 mm	5.43 mm	5.42 mm
		Max.	5.64 mm	5.52 mm	5.54 mm
Hardness	Not more than 4.0 Kgf		13.12 Kgf	20.37 Kgf	20.76 Kgf
Friability	Not more than 1.0 % w/w		0.26 % w/w	0.18% w/w	0.13 % w/w
Disintegration Time	Not more than 15.0 Minutes		06 Minutes 48 Sec.	06 Minutes 21 Sec.	06 Minutes 03 Sec
Average Weight	601.40 to 638.60 mg		623 mg	620.82 mg	614.56 mg
Uniformity of weight	Not more than 2 tablets in 20 deviates from the average weight by more than 5.0%.No tablet deviate from the average weight by more than 10.0 %.		Deviation -2.48 to +2.55 %	Deviation -0.92 to +1.38 %	Deviation -2.23 to +2.73 %

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Dissolution	Not less than 75.0% of the stated amount in 15 Minutes Stage:S1 Number tested :6 Each unit is not less than Q+5 Percent of the labelled content. Stage:S2 Number tested :6 Average of 12 units (S1+S2) is equal to or greater than Q, and no unit is less than Q-15 Percent of the labelled content. Stage:S3 Number tested :12 Average of 24 units (S1+S2+S3) is equal to or greater than Q, not more than 2 Units are less than Q-15 Percent of the lebelled content and no unit is less than Q-25 Percent of the labelled content.	Min:91.3 % Max. 99.6% Avg.: 95.7%	Min:93 .6% Max. 109.8% Avg.: 98.1%	Min: 94.0% Max. 109.7 % Avg.: 99.5%

Uniformity of dosage unit				
by Weight Uniformity	Acceptance value should be less than 15	1.5	1.50	3.20
Related substances (By TLC)				
Lithocholic acid	Not more than 0.1%	Not detected	Not detected	Not detected
Cholic acid	Not more than 0.5%	Not detected	Not detected	Not detected
Chenodeoxycholic acid	Not more than 1.5%	Not detected	Not detected	Not detected
Any other secondary impurity	Not more than 0.5%	Not detected	Not detected	Not detected
Assay: Each uncoated tablets contains:				
Ursodeoxycholic Acid IP…300 mg	92.5 to 107.5 %	101.5 %	100.0 %	99.0%
Microbial Limit Test				
Total Aerobic Bacterial Count	NMT 1000 cfu/gm	40 cfu/gm	30 cfu/gm	30 cfu/gm
Total Fungal Count	NMT 100 cfu/gm	< 10 cfu/g	< 10 cfu/g	< 10 cfu/g

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Pathogen *E. coli*	Should be Absent	absent	absent	absent

Conclusion: The manufacturing process for Ursodeoxycholic Acid Tablets 300 mg was successfully validated using a prospective approach. All three validation batches consistently met the predefined critical quality attributes (CQAs) and regulatory specifications, confirming the process is robust, reproducible, and suitable for routine commercial manufacturing.

Further work may focus on continued process verification (CPV) during commercial production to ensure sustained performance over time. Additionally, exploring process optimization using Quality by Design (QbD) tools and real-time monitoring technologies (e.g., PAT – Process Analytical Technology) can enhance control and reduce variability. Scaling to other dosage strengths or fixed-dose combinations may also be pursued based on this validated platform.

Refrences

1. Good Manufacturing Practices for Pharmaceutical Products. WHO Expert Committee on Specifications for Pharmaceutical Preparations (1992).32nd Report, WHO Technical Report Series no.823. Geneva: WHO, 14-96.
2. A WHO guide to GMP (1997); Requirements, part 2: Validation.
3. US Department of human and health services, Food and Drug administration, Center for drug evaluation and research (CDER), Center for biologics evaluation and research (CBER), Center for Veterinary medicine (CVM), Guidance for industry process validation general principles and practices, 2008; 1-19
4. Agalloco J. Validation: an unconventional review and reinvention; .PDA J. Pharm. Sci. Tech.1995; 49:175-179.
5. Frank T, Brooks B, Creekmore R. Quality risk management principles and industry case studies. Merck & Co; 2008.
6. Chapman KG. A History of Validation in United States, Part1; Pharm Tech.1991; 15:82-96.
7. Trubinski CJ. Rétrospective validation. In: Nash RA, Wachter AH, editors. Pharmaceutical process validation. New York (NY): Marcel dekkerInc; 2003. p. 31–57.
8. atto E, Okhamafe AO. An Overview of Pharmaceutical Validation and Process Controls in Drug Development. *Trop J Pharm Res*. 2002;1(2):115–22.
9. Nagavi BG. Pharmaceutical solid dosage form. *Indian J Pharm Educ Res*. 2012;46:5464.
10. Amidon GL, Shukla MP. Process validation of solid dosage form. *Res Dev*. 2010;5(29):1–7.
11. Chitlange SS, Pawar AS, Pawar HI, Bhujbal SS and Kulkarni A. A Validation 2006; 4:318-332.
12. Nash RA. and Wachter AH. *Pharmaceutical Process Validation An International Third Edition.* Revised and Expanded, Marcel Dekkar, Inc., New York 2003; 129:760-792.
13. Guganpreet K, Rana AC. The role of process validation in pharmaceutical industry. Int Res J Pharm. 2012;3(1):25–7.
14. Vandere GP, Sathe BS, Bharate SD. Prospective Process Validation/ Premarket Validation: a Focus on Drug Development. Pharma Times 2006; 38:20-38.
15. Chao AY, Forbes FJ, Johnson RF. Prospective Process Validation. In: Nash RA, Watcher AH, editors. Pharmaceutical Process Validation, New York: Marcel Dekker 2003; 47-69.
16. Amidon GL, Shukla MP. Process validation of solid dosage form. *Res Dev*. 2010;5(29):1–7.
17. Nandhakumar. An overview of pharmaceutical validation: Quality assurance view point. *IJRPC*. 2011;p. 15–21.
18. Trublnskl JC. Retrospective Process Validation. In: Nash RA, Watcher AH, editors.Pharmaceutical Process Validation. Marcel Dekker 2003; 3:71-77.
19. Himanshu, Pahuja S. A. Review on Pharmaceutical Process Validation. International Journal of Pharmacy, 2012; 3(7): 56-58.
20. Kiffer RG. Guidelines on general principles of process validation. PDA J Pharm Sci Tech 1995; 44(5): 249-55.
21. Pandita R., Rana AC, Seth N. Introduction and general overview of pharmaceutical process validation: review. International Research Journal of Pharmacy. 2012; 3(6): 60-64.
22. Chow S. Pharmaceutical validation and process controls in drug development. Drug Inf J 1997; 31: 1195-001.

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23. Gupta GD, Garg R and Aggarwal S. Guidelines on General Principles of Validation: Solid, Liquid and Sterile dosage forms 2008; 6:28-33.
24. Tandel MJ, Kumar J, Dedania R, Vadalia KR. Process Validation of Pyrazinamide Tablets: Review. International Journal of Advances in Pharmacy, Biology and Chemistry. 2012; 1(3): 342-353.
25. ICH Quality Guidelines (Q10). Pharmaceutical Quality System. London; 2006.
26. Rahul P. Process Validation of finasteride tablets. International journal of pharmaceutical chemical and biological sciences 2012; 2(1): 11-28.
27. Jain, N.K., A text book of Pharmaceutical Product development, CBS publisher, 2005, 525-533.
28. Nandha Kumar L. An overview of pharmaceutical validation- Quality Assurance view point. International journal of Research in pharmacy and chemistry 2011; 1(4): 1003-1014.
29. Vandana B Patel. Studies in prospective process validation of Cimetidine tablet dosage form. International journal of Research in pharmaceutical and biomedical sciences 2011; 2(4): 1823-1836.
30. Chawla Nirmaljot Singh. An Overview of Process validation in tablets. International research journal of pharmacy 2012; 3 (1): 114-116.
31. Sharma Tejal. Process validation: An Essential in the Pharmaceutical Industry. International Journal of Pharmaceutical Research and Development 2011; 3(10): 133-142.