

QUALITY RISK ASSESSMENT OF A DIRECT COMPRESSION TECHNOLOGY FOR LOZENGES CONTAINING AJANIA FRUTICULOSA (LEDEB.) POLJAK EXTRACT WITHIN THE QUALITY BY DESIGN FRAMEWORK

A. M. Jakiyanov¹, Z. B. Sakipova¹, Z. B. Allamberganova¹, A. Kadyrbay²,

R. I. Kulmanbetov¹, G. S. Ibadullayeva¹, M. K. Suleimenov^{1*}

¹ NJSC «S. D. Asfendiyarov Kazakh National Medical University», Kazakhstan, Almaty

² «Viva Pharm» LLP, Kazakhstan, Almaty

*Corresponding author

Abstract

Relevance. Direct compression enables lozenge manufacturing without wet granulation and drying. However, variability in the properties of herbal extracts may affect the reproducibility of critical quality attributes. Quality risk management within the Quality by Design framework supports systematic identification of variability sources and justification of a control strategy.

Objective. To identify and assess quality risks during the development of a direct compression technology for lozenges containing dry *Ajania fruticulosa* (Ledeb.) Poljak extract.

Materials and methods. Potential sources of variability were structured using an Ishikawa cause-and-effect diagram. Risks were ranked using Failure Mode and Effects Analysis. Severity, occurrence, and detectability were assessed using five-point scales, and Risk Priority Numbers (RPNs) were calculated. Residual risks were predicted by expert reassessment of occurrence and detectability under the proposed mitigation scenario, while severity scores remained unchanged.

Results. Thirty-six potential variability factors were identified, and seven priority failure modes were selected for Failure Mode and Effects Analysis. Initial RPNs ranged from 18 to 48. Powder blend segregation during feeding into the hopper zone had the highest initial RPN. Under the proposed mitigation scenario, predicted residual RPNs ranged from 6 to 24. Six of the seven failure modes were classified as low risk, including five initially classified as medium risk. Powder blend segregation remained a medium risk requiring continued monitoring.

Conclusions. The proposed control strategy provides a basis for further process development, technology transfer, and scale-up. Risk reduction represents an expert prediction and requires experimental confirmation through measurement of the corresponding critical quality attributes.

Keywords: Tablets; Plant Extracts, Risk Management, Quality Control, *Ajania fruticulosa*, Quality by Design, Ishikawa diagram, Failure Mode and Effects Analysis.

Introduction

The development of solid dosage forms requires a scientifically grounded and systematically organized approach that integrates formulation design, manufacturing process development, and a quality control strategy. In contemporary pharmaceutical development, the Quality by Design (hereinafter – QbD) paradigm provides a structured framework in which product quality is regarded not merely as the result of end-product testing, but

as the outcome of a comprehensive understanding of the formulation, manufacturing process, and sources of variability. Within this framework, the relationships between critical material attributes (hereinafter – CMAs), critical process parameters (hereinafter – CPPs), and critical quality attributes (hereinafter – CQAs) of the finished dosage form should be identified during the early stages of development and managed throughout the product lifecycle [1-3].

Quality risk management is a central element of QbD-based pharmaceutical development, as it enables systematic identification, evaluation, and control of factors that may affect product quality. According to the International Council for Harmonization (hereinafter – ICH) guideline Q9(R1), quality risk management comprises a systematic process for the assessment, control, communication, and review of risks to the quality of medicinal products. In this context, risk assessment tools are used to determine which material attributes and process parameters are most likely to influence CQAs and therefore require further investigation, monitoring, or control [2]. Cause-and-effect analysis and Failure Mode and Effects Analysis (hereinafter – FMEA) are among the most widely applied tools for this purpose, as they allow potential sources of variability to be structured, their impact to be evaluated, and appropriate control strategies to be developed during formulation and process development [4-8].

Direct compression is widely used for the manufacture of tablets and lozenges because of its technological simplicity, reduced number of unit operations, and omission of wet granulation and drying stages. These advantages make the method attractive from both technological and economic perspectives. However, the simplified nature of the process also increases its dependence on the intrinsic properties of the powder blend, since there are fewer intermediate processing steps capable of correcting suboptimal material behavior. Consequently, powder flowability, compressibility, particle-size distribution, moisture content, and segregation tendency may directly affect key CQAs of the finished dosage form, including mass uniformity, content uniformity, resistance to crushing, friability, and disintegration behavior [8-10].

The need for a risk-based development strategy is also relevant to directly compressed dosage forms containing plant-derived materials. A study of Atriplex halimus powder tablets examined particle size and compression force in relation to tablet properties [9], while research on Merremia tridentata extract tablets used formulation optimization to obtain acceptable tablet characteristics [10]. These studies support evaluating material attributes, formulation composition, and process parameters during the development of plant-based tablets. For the present *Ajania fruticulosa* formulation, their potential influence on CQAs was therefore considered during risk identification. Formulation and direct compression have also been investigated for non-herbal orally

disintegrating tablets, although these findings do not establish the properties of herbal extracts [11; 12].

In this regard, *Ajania fruticulosa* (Ledeb.) Poljak represents a promising plant-derived substance for further pharmaceutical development. This perennial species of the *Asteraceae* family is widely distributed in Kazakhstan, other regions of Central Asia, Mongolia and China. Phytochemical investigations of its aerial parts have reported the presence of flavonoids, terpenoids, phenolic acids, and sesquiterpenoid compounds, which supports its potential as a source of biologically active constituents for pharmaceutical applications [13-15]. Based on this phytochemical potential, previous formulation studies established the composition and preliminary technological parameters of lozenges containing dry *Ajania fruticulosa* extract using the QbD approach [13].

Nevertheless, although the formulation composition and preliminary technological parameters of these lozenges have been previously proposed, the quality-related risks associated with their manufacture by direct compression have not yet been sufficiently systematized. In particular, the material- and process-related factors that may affect the CQAs of the dosage form during formulation development, technology transfer, and scale-up require further identification, assessment, and prioritization. Such an assessment is necessary to support the development of a scientifically justified control strategy and to improve the robustness and reproducibility of the manufacturing process.

Therefore, the aim of the present study was to identify and assess quality-related risks associated with the development of a direct compression technology for lozenges containing dry *Ajania fruticulosa* extract within the QbD framework.

Materials and Methods

This study was designed as an pharmaceutical development study incorporating a structured expert-based quality risk assessment. The object of the study was the direct compression technology for lozenges containing dry *Ajania fruticulosa* extract. The methodological framework included the identification of potential sources of variability, ranking of quality-related risks, and assessment of residual risk.

Manufacturing of lozenges by direct compression

Lozenges were manufactured by direct compression according to the procedure disclosed in Republic of Kazakhstan utility-model patent No. 11229, dated 3 October 2025 [16]. Dry *Ajania fruticulosa* extract was used as the API at a content of 3.75 mg per dosage unit. Sorbitol, copovidone, talc, magnesium stearate, and peppermint oil were used

as excipients. Prior to processing, all solid components were passed through a 0.5 mm sieve. The API was initially blended with a portion of sorbitol until visual homogeneity was achieved. The remaining sorbitol, copovidone, peppermint oil, and talc were then added sequentially, while magnesium stearate was incorporated at the final blending stage. Final mixing was performed for 5-10 min at 30-40 °C, and the moisture content of the powder blend was maintained within the range of 2.5-3.0 %. Compression was carried out using a single-punch tablet press at a compression force of 15-30 kN to obtain flat cylindrical lozenges with an average mass of 250 mg. The reported parameter ranges were considered preliminary operating ranges. Their formal establishment as a Design Space using Design of Experiments was beyond the scope of the present study.

Risk assessment

Initial identification of potential risk sources was performed using cause-and-effect analysis and presented in the form of an Ishikawa diagram. The identified factors were classified into seven categories: materials, direct compression process, equipment, quality control, personnel, environmental conditions, and packaging. In total, 36 potential factors were initially identified across these categories [2].

Factors were retained for detailed FMEA ranking if they met at least one of the following criteria: direct potential impact on predefined CQAs, including uniformity of content, uniformity of mass, friability, resistance to crushing, and disintegration, association with the known technological variability of herbal extracts, relevance to the robustness of the direct compression process, or anticipated need for additional control during scale-up. Factors considered to have only indirect or minor influence were retained within the general control strategy but were not subjected to detailed Risk Priority Number (hereinafter – RPN) ranking [2; 17].

FMEA was selected as the quantitative risk-ranking tool because the study required a systematic comparison of multiple material- and process-related risk factors that may affect the quality of lozenges manufactured by direct compression. Unlike fault tree analysis, which is primarily used to investigate a defined failure event, and unlike Hazard Analysis and Critical Control Point (hereinafter – HACCP), which is mainly focused on the identification and control of critical control points, FMEA allows heterogeneous failure modes to be evaluated simultaneously according to several independent criteria [2; 17]. These criteria include severity of impact on CQAs (hereinafter – S), probability of occurrence

(hereinafter – O), and detectability (hereinafter – D). Higher D scores indicate a lower likelihood of detecting the failure before batch release.

The use of FMEA was therefore considered methodologically appropriate for this study because the manufacturing process involved a plant-derived extract with variable technological properties. Such variability may influence powder flow, compressibility, moisture sensitivity, and reproducibility of compression. FMEA enabled the transformation of qualitatively identified risk factors into a quantitative ranking system and provided a basis for prioritizing proposed risk mitigation measures. The sequential use of Ishikawa analysis and FMEA was applied to combine qualitative root-cause structuring with quantitative risk prioritization within the QbD framework.

For each potential failure mode, the possible consequences for CQAs, the most probable causes, and the existing control measures were identified. Risk was assessed using three criteria: S, O, and D. Each criterion was scored on a five-point scale, as presented in Table 1. Scoring was performed by an expert panel consisting of five specialists representing the academic and industrial partners of the study, namely the School of Pharmacy at KazNMU and Viva Pharm LLP. The panel members had combined expertise in formulation development, pharmaceutical technology, and quality control.

Panel members were selected based on their professional background in one of these areas and a minimum of five years of relevant practical experience. Three panel members were also co-authors of the manuscript and contributed, respectively, to scientific supervision, risk identification and scoring, and evaluation of the technological feasibility of the proposed risk mitigation measures from a manufacturing perspective. Initial scores were assigned independently and subsequently harmonized by consensus after discussion of the technological relevance of each failure mode, its expected impact on CQAs, and the ability of existing in-process controls to detect the failure before batch release. If consensus could not be reached, the higher score was retained as a conservative measure.

Study-specific five-point scales for severity, occurrence, and detectability were developed in accordance with the quality risk management principles of ICH Q9(R1), with reference to the risk-analysis approach described by Ccopa Ibarra et al. [2; 18]. The level descriptors were reformulated to reflect the CQAs relevant to direct-compression lozenge manufacturing, specifically uniformity of content,

uniformity of mass, friability, resistance to crushing, and disintegration, rather than the generic process descriptors provided in the source schemes.

The Risk Priority Number was calculated according to the following equation:

$$RPN = S \times O \times D$$

Risks were ranked according to their RPN values, and the need for proposed risk mitigation measures was determined in accordance with the classification presented in Table 2.

The effectiveness of the proposed risk mitigation measures was assessed by re-rating O and D under

the proposed mitigation scenario and by recalculating the RPN to determine residual risk. The severity score was kept constant for all failure modes, based on the methodological assumption that severity reflects the intrinsic impact of a failure on the affected CQA and is not altered by procedural or technological controls. The recalculated RPN values therefore represent expert-predicted residual risks expected after implementation of the proposed risk mitigation measures, rather than experimentally confirmed process-validation outcomes. Quantitative confirmation of mitigation effectiveness through direct CQA measurement was defined as a subsequent stage of process development.

Table 1. Severity, occurrence and detectability scales used in FMEA

Score	S – Impact on CQA	O – Probability of failure	D – Likelihood of detection
1	No impact on CQA	Highly unlikely	Deviation is easily detected
2	Minor impact on a single CQA	Rare	High probability of detection
3	Moderate impact, with possible deviations from acceptance criteria	Possible	Moderate probability of detection
4	Significant impact requiring rigorous in-process control	Highly probable and may occur frequently under insufficient CPP regulation, limited control barriers, and variable environmental conditions	Low probability of detection
5	Critical impact resulting in non-compliance	Almost inevitable and occurs systematically until formulation or process parameters are modified	Practically undetectable

Source: compiled by the authors

Table 2. Interpretation of Risk Priority Number and management actions

Risk zone	RPN range	Interpretation	Management action
Low	1-20	Risk is acceptable	Maintain existing control points and continue parameter monitoring
Medium	21-50	Risk requires management	Refine CMAs and CPPs, narrow tolerances, strengthen operational control, and conduct additional confirmatory testing where necessary
High	51-125	Risk is unacceptable	Propose risk mitigation measures, modify formulation or process parameters where necessary, revise the control strategy, and reassess RPN

Source: compiled by the authors

Ethical considerations

The study did not involve human participants, personal medical data or laboratory animals. Therefore, approval by an ethics committee was not required.

Results

The Ishikawa cause-and-effect analysis enabled the systematic identification of potential sources of variability during the development of lozenges containing dry *Ajania fruticulosa* extract by direct compression. A total of 36 potential factors were identified and grouped into seven categories: materials, direct compression process, equipment, quality control, personnel, environmental conditions, and packaging (Figure 1). Material-related factors included the technological properties of the API and excipients. The main CMAs of the dry *Ajania fruticulosa* extract were particle-size distribution, flowability, compressibility, hygroscopicity, and solubility.

Sorbitol, copovidone, talc, and magnesium stearate were also identified as potential sources of variability due to their influence on powder flow, interparticle interactions, adhesion behavior, lubrication efficiency, and compression performance.

Process-related factors were mainly associated with blending and compression. The CPPs included blending time, mixing intensity, component addition sequence, intermediate holding time of the powder blend, compression force, and mass-feed conditions. Equipment-related factors included blender geometry, technical condition of the tablet press, die and punch condition, sieve wear, and weighing accuracy. Environmental temperature and relative humidity were identified as additional factors because of their potential influence on the moisture content of the powder blend and the reproducibility of compression.

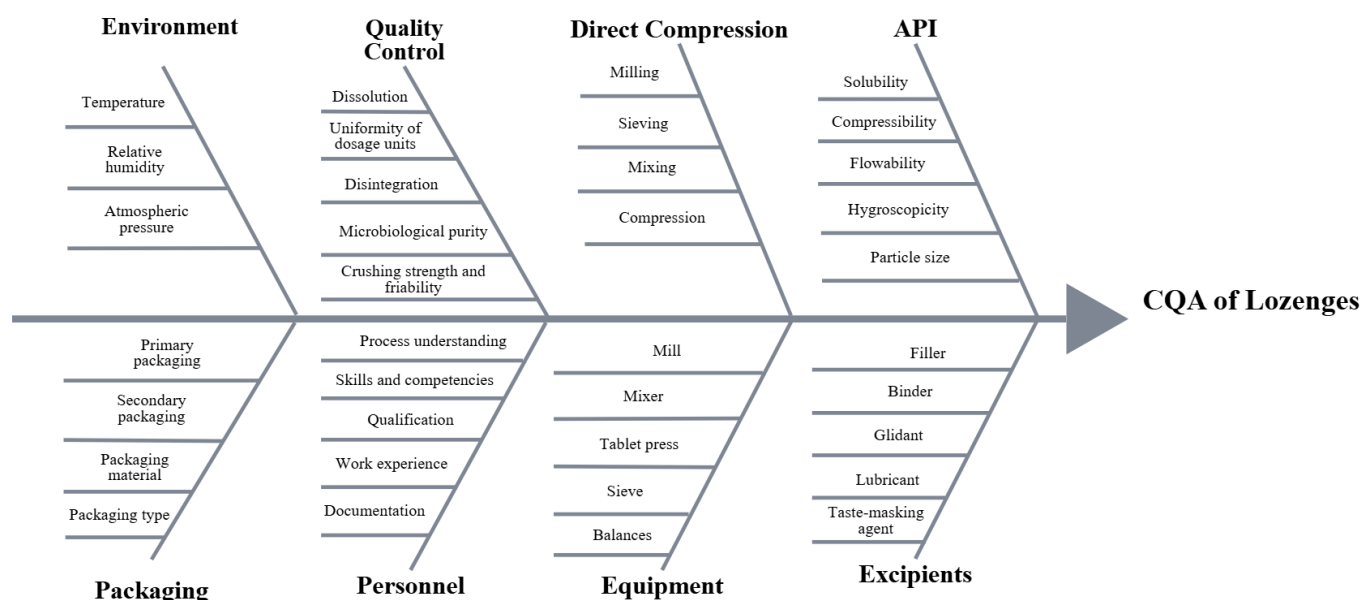


Figure 1. Ishikawa diagram for the identification of quality-risk sources during the development of lozenges by direct compression.

Source: compiled by the authors

Based on the Ishikawa analysis, seven priority failure modes were selected for detailed FMEA ranking. Selection was based on their direct potential impact on CQAs, relevance to the robustness of direct compression, and expected importance during technology transfer and scale-up. The selected failure modes were associated with uniformity of content, uniformity of mass, friability, resistance to crushing, and disintegration.

Initial RPN values for the selected failure modes ranged from 18 to 48 (Table 3). The highest initial RPN was observed for segregation of the powder blend during feeding into the hopper zone, which was rated at 48. Non-uniform distribution of the API in the powder blend and increased moisture content of the powder blend each exhibited an RPN of 36. Increased adhesion of the powder blend to blender walls and increased lozenge friability

were both quantified at 27. Variation in lozenge mass was assigned an RPN of 24. Insufficient resistance to crushing showed the lowest initial RPN among the selected priority failure modes, with a value of 18.

According to the predefined risk classification, six of the seven priority failure modes were assigned to the medium-risk zone before consideration of the proposed risk mitigation measures. One failure mode, insufficient resistance to crushing, was classified as low risk. No high-risk failure modes were identified.

Proposed risk mitigation measures were formulated for all selected priority failure modes. These measures included standardization of blending parameters, control of particle-size distribution, regulation of moisture content, optimization of the

component addition sequence, refinement of compression parameters, regulation of mass-feed conditions, and introduction of additional in-process control points. After re-rating occurrence and detectability under the proposed mitigation scenario, residual RPN values decreased for all evaluated failure modes and ranged from 6 to 24.

Under the proposed mitigation scenario, six of the seven priority failure modes were classified as low risk, including five initially classified as medium risk. Segregation of the powder blend during feeding into the hopper zone remained in the medium-risk zone, with a residual RPN of 24, and therefore required continued in-process monitoring. The complete distribution of S, O, D, and RPN values before and under the proposed mitigation scenario is presented in Table 3.

Table 3. Risk assessment of the technological stages of lozenge manufacturing by direct compression

№	Process stage	Failure mode	Affected CQA	Initial S/O/D/RPN	Proposed risk mitigation measures	Residual S/O/D/RPN	Residual risk zone
1	Preparation of powder blend for compression	Segregation of the powder blend during feeding into the hopper zone	Uniformity of content	4 / 4 / 3 / 48	Standardization of blending parameters, control of particle-size distribution, moisture content, and intermediate holding time of the powder blend	4 / 3 / 2 / 24	Medium risk, continued in-process monitoring required
2	Blending	Non-uniform distribution of the API in the powder blend	Uniformity of content	4 / 3 / 3 / 36	Optimization of the component addition sequence, regulation of blending time, and control of uniformity of content	4 / 3 / 1 / 12	Low risk, routine monitoring
3	Blending	Increased adhesion of the powder blend to blender walls	Uniformity of content	3 / 3 / 3 / 27	Moisture control and use of glidants at the optimal concentration	3 / 1 / 3 / 9	Low risk, routine monitoring
4	Preparation of powder blend	Increased moisture content of the powder blend	Disintegration, friability, uniformity of content	3 / 4 / 3 / 36	Introduction of a moisture-content control point and restriction of the CPP range	3 / 2 / 2 / 12	Low risk, routine monitoring

№	Process stage	Failure mode	Affected CQA	Initial S/O/D/RPN	Proposed risk mitigation measures	Residual S/O/D/RPN	Residual risk zone
5	Compression	Increased lozenge friability	Friability	3 / 3 / 3 / 27	Standardization of compression parameters and control of lozenge surface quality	3 / 3 / 1 / 9	Low risk, routine monitoring
6	Compression	Variation in lozenge mass	Uniformity of mass, dosage unit uniformity	4 / 3 / 2 / 24	Regulation of mass-feed parameters and periodic control of lozenge mass	4 / 2 / 1 / 8	Low risk, routine monitoring
7	Compression	Insufficient resistance to crushing	Resistance to crushing, friability	3 / 3 / 2 / 18	Optimization of compression force and control of binder content	3 / 2 / 1 / 6	Low risk, routine monitoring

*Note. The values were obtained by expert FMEA scoring. Residual RPN values represent expert-predicted risk levels after consideration of the proposed risk mitigation measures rather than experimentally validated process outcomes

Source: compiled by the authors based on Ishikawa analysis and FMEA scoring

Discussion

The present study established a quality-risk profile for lozenges containing dry *Ajania fruticulosa* extract manufactured by direct compression. The highest initial RPN was associated with segregation of the powder blend during feeding into the hopper zone, while non-uniform API distribution and increased moisture content were also identified as priority risks. These findings indicate that the main sources of variability were concentrated at the stages of blending, intermediate handling, feeding, and compression.

This risk hierarchy reflects the technological sensitivity of direct compression. The method requires stable flowability, compressibility, particle-size distribution, moisture content, and blend homogeneity. In the present formulation, these factors were especially important because the dosage form contained a low amount of dry *Ajania fruticulosa* extract, 3.75 mg per dosage unit. Therefore, even moderate segregation or local variability in the powder blend may affect uniformity of content.

The predominance of segregation-related risk can be explained by the multicomponent composition of the formulation and possible differences in particle size, density, morphology, and flow properties between the herbal API and excipients. Since segregation may occur after blending, it cannot be reliably corrected by final product testing alone.

This explains why this failure mode remained a medium residual risk after consideration of the proposed risk mitigation measures and requires continued monitoring during scale-up.

The present results differ from those reported by Kaljević et al. [8], who applied FMEA to compression-coated tablets with pulsatile carvedilol release. In that study, the main risks were associated with formulation variables affecting the release profile. In contrast, the highest-ranked risks in the present study were related to raw-material variability, powder blend behavior, and feeding reproducibility. This difference is mainly due to the nature of the API, since carvedilol is a well-characterized synthetic substance, whereas dry *Ajania fruticulosa* extract is a plant-derived material with more variable technological properties.

A similar distinction is observed in comparison with Naman et al. [12], who developed flavored paracetamol oral disintegrating mini-tablets using a risk-based QbD approach. Their risk assessment mainly focused on excipient selection and optimization of formulation and process variables. In the present work, the main risks were more closely related to the herbal API itself, particularly its influence on powder flow, moisture sensitivity, blend uniformity, and feeding behavior.

The increased risk associated with the herbal API is consistent with the technological limitations

of plant-derived extracts. Such materials may vary in residual moisture, hygroscopicity, particle morphology, particle-size distribution, bulk density, and adhesion tendency. These properties can impair flowability and compressibility, increase adhesion to equipment surfaces, and promote segregation. As a result, material-related and blending-related failure modes occupied the highest positions in the risk hierarchy.

The proposed risk mitigation measures reduced predicted RPN values for all selected failure modes. The greatest reductions were observed for non-uniform API distribution, increased moisture content, and variation in lozenge mass. These reductions were associated with optimization of the component addition sequence, regulation of blending time, moisture-content control, refinement of mass-feed conditions, and additional in-process controls. However, segregation during feeding remained a medium residual risk, indicating that procedural controls alone may not fully eliminate this failure mode.

Compared with previous studies on directly compressed herbal tablets, which mainly focused on formulation development and product characterization, the present work provides a structured quality-risk assessment for a low-dose herbal lozenge. The novelty of the study lies in the sequential use of Ishikawa analysis and FMEA, quantitative RPN-based prioritization, predicted residual risk assessment, and formulation of proposed risk mitigation measures within an ICH Q9(R1)-aligned QbD framework.

Overall, direct compression of lozenges containing dry *Ajania fruticulosa* extract requires enhanced control of both CMAs and CPPs. The proposed control strategy provides a scientific basis for further process development, documentation, technology transfer, and scale-up.

Limitations. FMEA scoring was based on expert judgment, and residual RPN values reflect predicted rather than experimentally confirmed risk reduction. In addition, the reported process ranges should be regarded as preliminary operating ranges rather than a formally established design space.

Conclusion

QbD-based quality risk assessment of the direct compression technology for lozenges containing dry *Ajania fruticulosa* extract was performed by combining an Ishikawa cause-and-effect diagram with FMEA. Seven priority failure modes were

identified, of which segregation of the powder mass during feeding into the hopper zone carried the highest initial risk. Corrective and preventive actions targeting critical material attributes and critical process parameters were predicted to reduce the RPN across all evaluated failure modes, resulting in six of the seven modes being classified as low risk, including five initially classified as medium risk, whereas segregation remained a medium residual risk requiring continued in-process monitoring. The resulting control strategy provides a scientifically justified basis for managing material and process-related variability during manufacturing. These expert-based predictions should be confirmed experimentally through direct measurement of the corresponding CQA during subsequent process development and scale-up.

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QUALITY BY DESIGN ТҰЖЫРЫМДАМАСЫ АЯСЫНДА AJANIA FRUTICULOSA (LEDEB.) POLJAK ЭКСТРАКТИСІ БАР СОРУҒА АРНАЛҒАН ТАБЛЕТКАЛАР ТЕХНОЛОГИЯСЫНЫҢ САПА ТӘУЕКЕЛДЕРІН БАҒАЛАУ

А. М. Джакиянов¹, З. Б. Сакипова¹, З. Б. Алламбергенова¹, А. Кадырбай²,
Р. И. Құлманбетов¹, Ф. С. Ибадуллаева¹, М. К. Сүлейменов^{1*}

¹ «С. Д. Асфендияров атындағы Қазақ ұлттық медицина университеті» КЕАҚ, Қазақстан, Алматы

² «Viva Pharm» ЖШС, Қазақстан, Алматы

*Корреспондент автор

Андатпа

Өзектілігі. Тікелей престоу соруға арналған таблеткаларды ылғалды түйіршіктеу және кептіру сатыларынсыз өндіруге мүмкіндік береді. Алайда өсімдік экстракттары қасиеттерінің өзгергіштігі сапаның критикалық көрсеткіштерінің қайталанымдылығына әсер етуі мүмкін. Quality by Design тұжырымдамасы аясында сапа тәуекелдерін басқару өзгергіштік көздерін жүйелі анықтауға және бақылау стратегиясын негіздеуге мүмкіндік береді.

Мақсаты. *Ajania fruticulosa* (Ledeb.) Poljak құрғақ экстракты бар соруға арналған таблеткаларды тікелей престоу технологиясын әзірлеу кезіндегі сапа тәуекелдерін анықтау және бағалау.

Материалдар мен әдістер. Өзгергіштіктің ықтимал көздері Исикава себеп-салдар диаграммасы арқылы жүйеленді. Тәуекелдер істен шығу түрлері мен олардың салдарын талдау әдісімен (FMEA) сараланды. Салдардың ауырлығы, туындау ықтималдығы және анықталу мүмкіндігі бес балдық шкалалар бойынша бағаланып, тәуекелдің басымдық саны (RPN) есептелді. Қалдық тәуекелдер ұсынылған шараларды ескере отырып, туындау ықтималдығы мен анықталу мүмкіндігін қайта сараптамалық бағалау арқылы болжанды. Салдардың ауырлық балдары өзгеріссіз қалдырылды.

Нәтижелер. Өзгергіштіктің 36 ықтимал факторы анықталып, FMEA үшін жеті басым істен шығу түрі таңдалды. Бастапқы RPN мәндері 18–48 аралығында болды. Ең жоғары бастапқы тәуекел ұнтақ қоспасын қоректендіргіш аймағына беру кезіндегі сегрегациямен байланысты болды. Ұсынылған шараларды қолдану сценарийінде болжамды қалдық RPN мәндері 6-24 аралығын құрады. Жеті істен шығу түрінің алтауы төмен тәуекел санатына жатқызылды; олардың бесеуі бастапқыда орташа тәуекел санатында болған. Ұнтақ қоспасының сегрегациясы орташа тәуекел деңгейінде қалып, әрі қарай бақылауды талап етеді.

Қорытынды. Ұсынылған бақылау стратегиясы технологияны әрі қарай әзірлеуге, трансферлеуге және масштабтауға негіз болады. Тәуекелдің төмендеуі сараптамалық болжамға негізделген және сапаның тиісті критикалық көрсеткіштерін өлшеу арқылы эксперименттік растауды қажет етеді.

Түйін сөздер: таблеткалар, өсімдік экстракттары, тәуекелдерді басқару, сапаны бақылау, *Ajania fruticulosa*, Quality by Design, Исикава диаграммасы, істен шығу түрлері мен олардың салдарын талдау.

ОЦЕНКА РИСКОВ КАЧЕСТВА ТЕХНОЛОГИИ ТАБЛЕТОК ДЛЯ РАССАСЫВАНИЯ С ЭКСТРАКТОМ *AJANIA FRUTICULOSA* (LEDEB.) POLJAK В РАМКАХ КОНЦЕПЦИИ QUALITY BY DESIGN

А. М. Джакиянов¹, З. Б. Сакипова¹, З. Б. Алламбергенова¹, А. Кадырбай²,
Р. И. Кульманбетов¹, Г. С. Ибадуллаева¹, М. К. Сулейменов^{1*}

¹ НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова»,
Казахстан, Алматы

² ТОО «Viva Pharm», Казахстан, Алматы

*Корреспондирующий автор

Аннотация

Актуальность. Прямое прессование позволяет получать таблетки для рассасывания без стадий влажного гранулирования и сушки. Однако вариабельность свойств растительных экстрактов может влиять на воспроизводимость критических показателей качества. Управление рисками в рамках концепции Quality by Design позволяет систематизировать источники вариабельности и обосновать стратегию контроля.

Цель. Идентифицировать и оценить риски качества при разработке технологии прямого прессования таблеток для рассасывания с сухим экстрактом *Ajania fruticulosa* (Ledeb.) Poljak.

Материалы и методы. Потенциальные источники вариабельности систематизированы с помощью причинно-следственной диаграммы Исикавы. Ранжирование рисков выполнено методом анализа видов и последствий отказов (FMEA). Тяжесть последствий, вероятность возникновения и обнаруживаемость оценивали по пятибалльным шкалам с расчётом приоритетного числа риска (RPN). Остаточные риски прогнозировали путём повторной экспертной оценки вероятности возникновения и обнаруживаемости с учётом предложенных мер; тяжесть последствий оставляли неизменной.

Результаты. Выявлены 36 потенциальных факторов вариабельности, из которых для FMEA отобраны семь приоритетных режимов отказа. Исходные значения RPN составили 18–48. Наибольший риск связан с сегрегацией порошковой смеси при подаче в зону питателя. В сценарии применения предложенных мер прогнозируемые остаточные значения RPN составили 6–24. Шесть из семи режимов отказа отнесены к области низкого риска, включая пять, первоначально классифицированных как средний риск. Сегрегация смеси сохранила средний уровень риска и требует дальнейшего контроля.

Выводы. Предложенная стратегия контроля служит основой для дальнейшей разработки, трансфера и масштабирования технологии. Снижение риска основано на экспертном прогнозе и требует экспериментального подтверждения посредством измерения соответствующих критических показателей качества.

Ключевые слова: таблетки, растительные экстракты, управление рисками, контроль качества, *Ajania fruticulosa*, Quality by Design, диаграмма Исикавы, анализ видов и последствий отказов.

АВТОРЛАР ТУРАЛЫ

Джакиянов Амангельды Муратович – Фармация мектебінің биотехнология және жалпы химиялық технология кафедрасының ассистент-профессоры, С. Д. Асфендияров атындағы Қазақ ұлттық медицина университеті, Қазақстан, Алматы; e-mail: dzhakiyanov.a@kaznmu.kz; ORCID: <https://orcid.org/0000-0001-5239-9429>.

Сакипова Зурияда Бектемировна – фармация ғылымдарының докторы, профессор, Фармация мектебінің деканы, С. Д. Асфендияров атындағы Қазақ ұлттық медицина университеті, Қазақстан, Алматы; e-mail: sakipova.z@kaznmu.kz; ORCID: <https://orcid.org/0000-0003-1400-1971>.

Алламбергенова Зоя Бакбергенқызы – PhD, инженерлік пәндер кафедрасының ғылыми атағы жоқ қауымдастырылған профессоры, С. Д. Асфендияров атындағы Қазақ ұлттық медицина

университеті, Қазақстан, Алматы; e-mail: allambergenova.z@kaznmu.kz; ORCID: <https://orcid.org/0000-0002-0801-0508>.

Кадырбай Аршын – «Viva Pharm» ЖШС фармацевтикалық әзірлемелер бөлімінің жетекшісі, Қазақстан, Алматы; e-mail: akadyrbai@vivapharm.kz; ORCID: <https://orcid.org/0000-0002-5288-6742>.

Құлманбетов Руслан Исатайұлы – м.ғ.к., ғылыми атағы жоқ қауымдастырылған профессор, ортодонтия кафедрасының меңгерушісі, С. Д. Асфендияров атындағы Қазақ ұлттық медицина университеті, Қазақстан, Алматы; e-mail: kulmanbetov.r@kaznmu.kz; ORCID: <https://orcid.org/0000-0002-9631-0112>.

Ибадуллаева Ғалия Сәруарқызы – PhD, қауымдастырылған профессор, фармацевтикалық технология кафедрасының профессоры, Фармация мектебі, «С. Д. Асфендияров атындағы Қазақ ұлттық медицина университеті» КеАҚ, Қазақстан, Алматы; e-mail: arujan-d@mail.ru; ORCID: <https://orcid.org/0000-0002-1268-9867>.

Сүлейменов Марат Камытбекұлы – хат-хабарға жауапты автор, биология ғылымдарының кандидаты, биотехнология және жалпы химиялық технология кафедрасының ғылыми атағы жоқ қауымдастырылған профессоры, С. Д. Асфендияров атындағы Қазақ ұлттық медицина университеті, Қазақстан, Алматы; e-mail: suleimenov.m@kaznmu.kz; ORCID: <https://orcid.org/0009-0005-6902-6262>.

ОБ АВТОРАХ

Джакиянов Амангельды Муратович – ассистент-профессор кафедры биотехнологии и общей химической технологии Школы Фармации, НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова», Казахстан, Алматы; e-mail: dzhakiyanov.a@kaznmu.kz; ORCID: <https://orcid.org/0000-0001-5239-9429>.

Сакипова Зуриядда Бектемировна – д.фарм.н., профессор, декан Школы Фармации, НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова», Казахстан, Алматы; e-mail: sakipova.z@kaznmu.kz; ORCID: <https://orcid.org/0000-0003-1400-1971>.

Алламбергенова Зоя Бакбергенқызы – PhD, ассоциированный профессор без ученого звания кафедры инженерных дисциплин, НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова», Казахстан, Алматы; e-mail: allambergenova.z@kaznmu.kz; ORCID: <https://orcid.org/0000-0002-0801-0508>.

Кадырбай Аршын – руководитель отдела фармацевтических разработок ТОО «Viva Pharm», Казахстан, Алматы; e-mail: akadyrbai@vivapharm.kz; ORCID: <https://orcid.org/0000-0002-5288-6742>.

Кульманбетов Руслан Исатаевич – к.м.н., ассоциированный профессор без ученого звания, заведующий кафедрой ортодонтии, НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова», Казахстан, Алматы; e-mail: kulmanbetov.r@kaznmu.kz; ORCID: <https://orcid.org/0000-0002-9631-0112>.

Ибадуллаева Ғалия Сәруарқызы – PhD, ассоциированный профессор, профессор кафедры фармацевтической технологии Школы Фармации, НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова», Казахстан, Алматы; e-mail: arujan-d@mail.ru; ORCID: <https://orcid.org/0000-0002-1268-9867>.

Сүлейменов Марат Камытбекович – корреспондирующий автор, к.б.н., ассоциированный профессор без ученого звания кафедры биотехнологии и общей химической технологии, НАО «Казахский национальный медицинский университет имени С. Д. Асфендиярова», Казахстан, Алматы; e-mail: suleimenov.m@kaznmu.kz; ORCID: <https://orcid.org/0009-0005-6902-6262>.

ABOUT THE AUTHORS

Jakiyanov Amangeldy Muratovich – Assistant Professor, Department of Biotechnology and General Chemical Technology, School of Pharmacy, S. D. Asfendiyarov Kazakh National Medical University, Kazakhstan, Almaty; e-mail: dzhakiyanov.a@kaznmu.kz; ORCID: <https://orcid.org/0000-0001-5239-9429>.

Sakipova Zuriadda Bektemirovna – Doctor of Pharmaceutical Sciences, Professor, Dean of the School of Pharmacy, S. D. Asfendiyarov Kazakh National Medical University, Kazakhstan, Almaty; e-mail: sakipova.z@kaznmu.kz; ORCID: <https://orcid.org/0000-0003-1400-1971>.

Allambergenova Zoya Bakbergenqyzy – PhD, Associate Professor without an academic title, Department of Engineering Disciplines, S. D. Asfendiyarov Kazakh National Medical University, Kazakhstan, Almaty; e-mail: allambergenova.z@kaznmu.kz; ORCID: <https://orcid.org/0000-0002-0801-0508>.

Kadyrbay Arshyn – Head of Pharmaceutical Development, Viva Pharm LLP, Kazakhstan, Almaty; e-mail: akadyrbai@vivapharm.kz; ORCID: <https://orcid.org/0000-0002-5288-6742>.

Kulmanbetov Ruslan Isatayevich – Candidate of Medical Sciences, Associate Professor without an academic title, Head of the Department of Orthodontics, S. D. Asfendiyarov Kazakh National Medical University, Kazakhstan, Almaty; e-mail: kulmanbetov.r@kaznmu.kz; ORCID: <https://orcid.org/0000-0002-9631-0112>.

Ibadullayeva Galiya Saruarkyzy – PhD, Associate Professor, Professor of the Department of Pharmaceutical Technology, School of Pharmacy, S. D. Asfendiyarov Kazakh National Medical University, Kazakhstan, Almaty; e-mail: arujan-d@mail.ru; ORCID: <https://orcid.org/0000-0002-1268-9867>.

Suleimenov Marat Kamytbekovich – Corresponding author, Candidate of Biological Sciences, Associate Professor without an academic title, Department of Biotechnology and General Chemical Technology, S. D. Asfendiyarov Kazakh National Medical University, Kazakhstan, Almaty; e-mail: suleimenov.m@kaznmu.kz; ORCID: <https://orcid.org/0009-0005-6902-6262>.

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