p-ISSN : 2788-5569 | e-ISSN : 2788-5445
DOI(Journal): 10.31703/gpsr
DOI(Volume): 10.31703/gpsr/.2024(IX)
DOI(Issue): 10.31703/gpsr.2024(IX.I)

www.gicdrjournal.com
Global Pharmaceutical Sciences Review
GPSR

GPSR

GLOBAL PHARMACEUTICAL SCIENCES REVIEW

VOL. IX, ISSUE I, WINTER (MARCH-2024)

HumanityPublications
sharing research
www.humapub.com
US | UK | Pakistan

Double-blind Peer-review Research Journal
www.gpsrjournal.com

HumanityPublications
sharing research
www.humapub.com
US | UK | Pakistan

Humanity Publications
(HumaPub)
www.humapub.com
Doi: https://dx.doi.org/10.31703

www.gpsrjournal.com
Global Pharmaceutical Sciences Review
GPSR

Article Title

A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations

Global Pharmaceutical Sciences Review
p-ISSN: 2788-5569 e-ISSN: 2788-5445
DOI(journal): 10.31703/gpsr
Volume: IX (2024)
DOI (volume): 10.31703/gpsr.2024(IX)
Issue: (Winter-March 2024)
DOI(Issue): 10.31703/gpsr.2024(IX-I)
Home Page
www.gpsrjournal.com
Volume: IX (2024)
https://www.gpsrjournal.com/Current-issues
Issue: I-Winter (March-2024)
https://www.gpsrjournal.com/Current-issues/9/1/2024
Scope
https://www.gpsrjournal.com/about-us/scope
Submission
https://humaglobe.com/index.php/gpsr/submissions
Google Scholar

Visit Us

Abstract

This review article investigates how Quality by Design (QbD) ideas are used in different pharmaceutical development processes, such as the creation of analytical methods, formulation optimization, and nanoparticle production. In order to improve product quality, reliability, and regulatory compliance, it covers a variety of studies that use QbD approaches. Critical quality attributes and process variables are discovered and optimized to meet desired product characteristics through systematic methodologies such as central composite design, factorial design, and response surface analysis. The experiments demonstrate the adaptability and effectiveness of the QbD strategy in pharmaceutical development by examining a range of drug delivery systems, including lipid nanoparticles and fast-dissolving tablets. The significance of QbD is emphasized in the article as a means of guaranteeing uniform product quality, fulfilling regulatory obligations, and enhancing patient outcomes.

Keywords: Quality by Design, Formulation Development, Design Space, Pharmaceuticals.

Authors:

Aqsa Qaisar: (Coprrespondant author)
Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.
(Email: aqsa.qaisar20gmail.com)
Maryam Sikandar: Graduate,Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.
Rehan Rustam: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.
Afifa Uppal: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.
Muhammad Adnan: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.
Zahid Ali: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.

Pages: 1-9
DOI: 10.31703/gpsr.2024(IX-I).01
DOI link: https://dx.doi.org/10.31703/gpsr.2024(IX-I).01
Article link: http://www.gpsrjournal.com/article/A-b-c
Full-text Link: https://gpsrjournal.com/fulltext/
Pdf link: https://www.gpsrjournal.com/jadmin/Auther/31rvIolA2.pdf

Humanity Publications (HumaPub)
www.humapub.com
Doi: https://dx.doi.org/10.31703

Citing this Article

01		A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations						
		Author	Aqsa Qaisar Maryam Sikandar Rehan Rustam Afifa Uppal Muhammad Adnan Zahid Ali		DOI	10.31703/gpsr.2024(IX-I).01		
Pages		1-9	Year	2024	Volume	IX	Issue	I
Referencing & Citing Styles	APA	Qaisar, A., Sikandar, M., Rustam, R., Uppal, A., Adnan, M., & Ali, Z. (2024). A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations. *Global Educational Studies Review*, *IX*(I), 1-9. https://doi.org/10.31703/gpsr.2024(IX-I).01						
	CHICAGO	Qaisar, Aqsa, Maryam Sikandar, Rehan Rustam, Afifa Uppal, Muhammad Adnan, and Zahid Ali. 2024. "A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations." *Global Educational Studies Review* IX (I):1-9. doi: 10.31703/gpsr.2024(IX-I).01.						
	HARVARD	QAISAR, A., SIKANDAR, M., RUSTAM, R., UPPAL, A., ADNAN, M. & ALI, Z. 2024. A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations. *Global Educational Studies Review,* IX**,** 1-9.						
	MHRA	Qaisar, Aqsa, Maryam Sikandar, Rehan Rustam, Afifa Uppal, Muhammad Adnan, and Zahid Ali. 2024. 'A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations', *Global Educational Studies Review*, IX: 1-9.						
	MLA	Qaisar, Aqsa, et al. "A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations." *Global Educational Studies Review* IX.I (2024): 1-9. Print.						
	OXFORD	Qaisar, Aqsa, et al. (2024), 'A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations', *Global Educational Studies Review,* IX (I), 1-9.						
	TURABIAN	Qaisar, Aqsa, Maryam Sikandar, Rehan Rustam, Afifa Uppal, Muhammad Adnan, and Zahid Ali. "A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations." *Global Educational Studies Review* IX, no. I (2024): 1-9. https://dx.doi.org/10.31703/gpsr.2024(IX-I).01.						

e-ISSN: 2788-5445 Volume: IX (2024) Issue: I-Winter (March-2024) p-ISSN: 2788-5569

Global Pharmaceutical Sciences Review
www.gpsrjournal.com
DOI: http://dx.doi.org/10.31703/gpsr

Pages: 1-9 URL: https://doi.org/10.31703/giidr.2024(IX-I).01 Doi: 10.31703/gpsr.2024(IX-I).01

Title

A Comprehensive Review on Implementation of Quality by Design in Varied Pharmaceutical Formulations

Abstract

This review article investigates how Quality by Design (QbD) ideas are used in different pharmaceutical development processes, such as the creation of analytical methods, formulation optimization, and nanoparticle production. In order to improve product quality, reliability, and regulatory compliance, it covers a variety of studies that use QbD approaches. Critical quality attributes and process variables are discovered and optimized to meet desired product characteristics through systematic methodologies such as central composite design, factorial design, and response surface analysis. The experiments demonstrate the adaptability and effectiveness of the QbD strategy in pharmaceutical development by examining a range of drug delivery systems, including lipid nanoparticles and fast-dissolving tablets. The significance of QbD is emphasized in the article as a means of guaranteeing uniform product quality, fulfilling regulatory obligations, and enhancing patient outcomes.

Contents

Keywords:

Quality by Design, formulation Development, Design Space, Pharmaceuticals

Authors:

Aqsa Qaisar: (Coprrespondant author)
Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.
(Email: aqsa.qaisar20gmail.com)

Maryam Sikandar: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.

Rehan Rustam: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.

Afifa Uppal: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.

Muhammad Adnan: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.

Zahid Ali: Graduate, Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.

Introduction

According to its description, QbD is "a systematic method for the development that starts with predefined objectives and emphasizes understanding of the process, material, and product as well as the involved process control. It is based on science and risk management of quality."

Dr. Juran argues that a product's design must take quality into account and that the majority of quality-related issues and crises stem from the original design of the product (Yu et al., 2014). The overarching idea is that capital allocation and manufacturing should happen once quality has been established (Grangeia et al., 2020). In practical terms, this means that businesses should begin by defining their quality objectives, creating features for their goods that help them meet these objectives, creating processes that can produce these products, and setting up controls that allow for consistent operation (Grangeia et al., 2020). As a result, the goal of QbD is to reliably and effectively meet customer needs. This is a different viewpoint from quality improvement, which is concentrated on resolving long-term issues and

minimizing process-inherent normal causes of variability after manufacturing begins (Grangeia et al., 2020)

Three distinct criteria were established by ICH to help integrate quality into pharmaceutical development. These consist of the ICH Q8, Q9 including Q10 recommendations, which work in concert to enhance quality improvement (Beg et al., 2019). ICH Q8 QbD wants us to realize that development is a systematic process that is based on science and risk management of high quality, starts with established aims, and stresses understanding the process, product as well and process control (Patil & Pethe, 2013)

Table 1

Quality By Design Parameters and their components

QBD parameter	Components
Quality Target Profile Product contents	Dosage form, administration methods, dosage strength(s), and so on (Zhang & Mao, 2017).
Critical Quality Attributes (CQAs)	These are characteristics of output items, like a finished pharmaceutical product, that are physical, chemical, biological, or microbiological (Zhang & Mao, 2017).
Critical Material Attributes (CMA)	These comprise material biological, chemical, physical, or microbiological properties (Zhang & Mao, 2017).
Critical Process Parameters (CPPs)	Variables that are tracked either after or before a process have a major impact on the final product appearance, yield, and purity (Zhang & Mao, 2017).

Different from CQAs, CMAs are identified as part of the product design and understanding phase in the Quality by Design method. CQAs are for output materials, while CMAs are for raw materials like drug compounds, in-process materials, and excipients. For a step in the downstream manufacturing process, an intermediate's CQA could become its CMA (Zhang & Mao, 2017). According to QbD, Critical material and process attributes can differ among the defined Design Space without affecting Critical quality attributes; as a result, the finished product's quality will fulfill the QTPP (Zhang & Mao, 2017) Qbd is a concept that promotes the application of science-based production concepts and risk management by the pharmaceutical sector to develop an understanding of products and processes, ultimately ensuring product quality (Mishra et al., 2018). Authorities including ICH and the Food and FDA are actively promoting QbD with the aim of reducing the escalating expenses associated with development and the regulatory obstacles that impede creativity and innovation (Mishra et al., 2018).

Method

Our research is an extensive analysis of the literature on the application of design software quality assurance in the creation of pharmaceuticals and the benefits attained via the usage of Quality by design approach. Our study included only those studies where QBD is used in the manufacturing of pharmaceuticals and excluded the rest. The primary goal is to determine how QBD is used in the development of pharmaceutical goods and what benefits it imposes.

Developing Pharmaceutical Formulations with Quality by Design

Using a QbD Methodology to Validate Ceftriaxone Sodium and Create HPLC Methods

In the process of developing analytical methods, the study was performed for the idea of ensuring product quality and regulatory compliance through Quality by Design, it emphasizes the importance of QbD concepts developed from ICH recommendations (Patel et al., 2021) They provided an explanation of the supplies, tools, and chromatographic settings used in the creation of the Chromatography technique that is High-Performance Liquid for ceftriaxone sodium in drug formulations

(Patel et al., 2021). The paper determines crucial factors influencing method performance, such as buffer solution pH and mobile phase composition, by factorial design and response surface analysis. It explains how the experiment is conducted, how optimization is done, and how the robustness and roughness of the procedure are assessed. The proven HPLC technique exhibits linearity, accuracy, precision, sensitivity, and appropriateness for ceftriaxone sodium testing (Patel et al., 2021)

Two crucial components of the process, the mobile phase, stationary phase, and pH, are centrally planned to produce an efficient experimental design that is described.

utilizing the 11.0 edition of the Design Expert program. The technique validation parameters fell within the permitted range as per the guidelines set forth by ICH. (7) The qbd importance in the advancement of analytical techniques is highlighted and provides insights into reliable and effective HPLC techniques that may find use in the pharmaceutical industry for compliance and quality control (Patel et al., 2021).

Qbd Approach in Formulation & Evaluation of Fast Dissolving Tablet Montelukast Sodium by Using Qbd Approach

The goal of the current studies was to create fast-dissolving tablets using the quality-by-design method. The essential qualities of the product are connected to important material and process factors (Bhusnure et al., 2015). Understanding products and processes reduces variability, which leads to increased productivity, lower risk, and improved quality. The study was used to propose the manufacture of a Montelukast sodium fast-dissolving tablet in order to improve patient compliance and product quality. The leukotriene receptor antagonist montelukast sodium has a 63% bioavailability and is used to treat asthma. Usually, oral administration is used. It showed high first-pass metabolism & very poor rate of dissolution. Anti-asthmatic drug Montelukast sodium has low bioavailability. Montelukast sodium Fast-dissolving tablets were developed, optimized, and characterized by using 32 factorial designs. The influences mainly interactive were tested using a statistical model (Bhusnure et al., 2015). The software was used to create the response surface plots to analyze how independent factors affected the response. Every batch was made by direct compression. Precompression characteristics, such as angle of repose, bulk density, tapered density, Hauser's ratio, post-compression characteristics, Carr's compressibility index, and such as drug homogeneity, hardness, and friability were assessed for tablets. Prior to the tablet formulation, to verify the compatibility of excipients IR spectroscopy investigations were also carried out (Bhusnure et al., 2015).

Results of the factorial design showed that variables that are dependent, disintegration time, are highly influenced by the amount of super disintegrant. Disintegration time is delayed by increasing an excipient's concentration (Bhusnure et al., 2015).

Creation of Nanoparticles Loaded with Sorafenib to Enhance Oral Bioavailability

Utilizing a process known as nanoparticulation utilizing fat and supercritical fluid (NUFSTM), researchers were able to create sorafenib nanoparticles that would improve the anticancer drug's low gastrointestinal absorption (Park et al., 2019). The formulation variables, such as poloxamer, polyvinyl pyrrolidone K30 (PVP), and hydroxypropyl methylcellulose (HPMC), optimization was done using the QbD technique. The size of the nanoparticles, the rate of dissolution at different times, the profiles of drug concentrations, and the maximum concentration of the drug were the main response variables examined (Park et al., 2019). The findings showed that while poloxamer and HPMC at higher concentrations reduced the size of the nanoparticles, PVP had a negative impact on drug dissolution and HPMC and poloxamer had a good effect (Park et al., 2019).

The modified sorafenib formulation showed higher levels in the blood, showing increased absorption than the reference tablet, according to in vivo pharmacokinetic experiments conducted in beagle dogs (Park et al., 2019). The work emphasizes how crucial a systematic formulation design is to comprehending how formulation variables affect the properties of poorly soluble therapeutic nanoparticles (Park et al., 2019).

Producing an Efavirenz-Loaded Nanoformulation: Investigating Safety in Vivo and Characterizations

In order to guarantee product quality, this study developed nanostructured lipid carriers encasing efavirenz using the Quality by Design methodology. Initially, to identify and categorize risk factors risk assessment methods were used (Gurumukhi & Bari, 2020).

This study utilized a central composite design rotatable for the examination of the effects of critical material and critical process attributes. Critical attributes of the material included combinations of solids and lipids including stabilizers (Gurumukhi & Bari, 2020). The statistical significance of the data was verified by analysis of variance (ANOVA). The intended reactions are used as the basis for determining the best formulation that satisfies quality standards. This formulation was then lyophilized and put through solid-state characterization, which allowed TEM imaging to reveal the spherical particle morphologies of NLC. The change of EF from a crystalline to an amorphous state in NLC was shown by DSC and PXRD. The results of 1HNMR and FTIR studies, respectively, indicated a lack of intermolecular hydrogen bonding and molecular interactions with the lipidic environment. In vitro drug release experiments using a

Higuchi-matrix mechanism showed a 91.21% release during a 24-hour period (Gurumukhi & Bari, 2020). In comparison to conventional formulations, in vivo pharmacokinetic studies showed a 2.95 times increase in relative BA which is a fraction of the drug reaching the systematic circulation and a decrease in liver toxicity for EF encapsulated in NLC. According to the study's findings, the QbD-based strategy successfully guaranteed product quality, producing highly promising nanocarriers with strong drug encapsulation capacity that improve bioavailability and validate the safety of EF-NLC with promising acceptable parameters (Gurumukhi & Bari, 2020).

Carbopol Transgel Formulation Pharmacokinetic Assessment, Characterization, and Therapeutic Efficacy in Diabetes Patients via Qbd Approach

Recently a study was performed to develop a transdermal system that can facilitate the absorption of Pioglitazone via the skin route and encapsulated in Carbopol transgel (Prasad et al., 2014). The developed formulation was optimized using qbd method and percentage entrapment, transdermal flux, and particle size were found. The study showed excellent carriers for delivery with more encapsulation, and improved flux value found that the absorption from skin was high with final formulation.(Prasad et al., 2014) The article "Optimization of Carbopol-based Transgel for Pioglitazone Delivery: A Proniosomal Approach" delves into the innovative realm of transdermal drug delivery systems, specifically focusing on the optimization and evaluation of proniosomal formulations for pioglitazone delivery. By incorporating carbopol-based transgels and proniosomes, the study showcases innovative formulation strategies to enhance drug delivery efficiency.(Prasad et al., 2014) Carbopols, known for their unique properties in forming microgel systems, are explored for their potential in transdermal gel formulations, while proniosomes offer a versatile platform for encapsulating both lipophilic and hydrophilic drugs. Pro-niosome led to transdermal enhancement by 3.16 which is more than that of PZ-controlled formulation and confirmation was done with laser scanning microscopy. In vivo, PK results showed significantly high bioavailability compared to tablet formulation. It showed better anti-diabetic activity than a marketed tablet and proved to be an efficient pioglitazone delivery carrier through the skin.(Prasad et al., 2014)

Qbd in Skin Cancer Treatment by Production of Lipid Nanoparticles using High-Pressure Homogenization

The goal of this project is to combine the benefits of lipid-based nanoparticles with the Quality by Design methodology to create a new medication system that can treat aktinic keratosis and skin cancer. Because lipid nanoparticles can penetrate the skin more deeply and get beyond the intricate structure of the skin barrier, they are among the most effective choices for the topical treatment of skin problems.(Amasya et al., 2019) All of the product's variables should be explained because the formulation creation process involves complicated variables including raw materials, active compounds, and production techniques. In order to accomplish a time- and money-saving procedure guaranteeing a product of high quality, the QbD approach was also effectively employed.(Amasya et al., 2019)

The following QbD procedures were used to create and characterize 5-fluorouracil loaded with lipid nanoparticles. Human keratinocyte and epidermoid cancer cell culture investigations were used to establish the cytotoxicity profiles of the ideal NLC.(Amasya et al., 2019) Compared to free 5-FU, optimal NLC exhibited a much greater anticancer impact on epidermal cell carcinoma and less cytotoxicity on human keratin cells. For simplicity of application, optimal NLC was developed in a hydrogel formulation with the right viscosity, pH, occlusive and mechanical qualities, and patient compliance.(Amasya et al., 2019)

The study's findings demonstrated that using artificial neural networks in conjunction with QbD guided formulation development. A new semisolid dosage form enriched with NLC was created, showing promise for the topical treatment of skin malignancies.(Amasya et al., 2019)

QBD-Based Development of HPLC Method for the Estimation of Eco-Friendly Nisoldipine

This study focuses on the HPLC method applied to nisoldipine (NLD) for quantification in bulk and nanoformulations using Qbd principles The design of experiments was used to idealize the method, where method critical factors. (13) were selected using a Taguchi orthogonal array procedure. The selection of variables was further performed using a Box Behnken procedure to

obtain optimal color indices. The method showed good linearity, sensitivity, precision, accuracy, specificity, and robustness according to regulatory guidelines. QbD principles played a key role in process initialization, risk assessment, diagnostic testing, and optimization to ensure a broad understanding of process performance. (13) Furthermore, the process routine proved to be specific for NLD in the presence of degradation products, which is important for accurate dosing. (13) This application required calculating the chemical composition of NLD nanosuspensions and studying in-vitro dissolution. The evaluation with green assessment tools showed that the developed method outperformed the reported methods in terms of environmental performance. (13)

Qbd in Melt Extrusion Technology for Continuous Manufacturing Delayed Release Pellets of Ketoprofen

This work explores a new approach for thermal extraction-based continuous delayed curing. To maximize the quality of medication release, it examines a number of variables, including drug concentration, stearic acid (SA) content, and tablet size. (14) Throughout production, real-time monitoring is used to provide quality control. The outcomes show that the method has the potential to produce pharmaceutical formulations that are durable since they show effective drug release under simulated gastrointestinal circumstances.

Using an experimental system (DOE) methodology was used to identify optimal chemicals and manufactured areas consistent with standards set by the U.S. Department of Agriculture. Manufacturers (USP) established meets. (14) This method allows real-time monitoring of critical parameters such as drug concentration and tablet size, ensuring consistent quality throughout production. (14) The study establishes the feasibility of continuing melt extrusion to produce longer-lasting tablet releases and emphasizes the ability to integrate continuous manufacturing within the pharmaceutical industry. (14)

Considerating Qbd in Developing a Tablet from Double Layered into a Single-Layered Tablet with Amlodipine and Telmisartan

Using a quality-by-design methodology, the study sought to create a Mono-layered Twynstar tablet that contained amlodipine and telmisartan. Critical parameters influencing drug quality and formulation were determined through risk assessment tools such as failure mode, analysis of effect, and preliminary hazard. The approach to formulation was optimized through the design of experiments, and then the design space was developed (Kim & Park, 2022). This space was used to prepare the single-layered tablets, which were then assessed for a number of characteristics including hardness, friability, and disintegration (Kim & Park, 2022). The double-layered tablets were found to be bioequivalent in beagle dogs through pharmacokinetic studies. For patients who need this combination therapy, the single-layered formulation showed increased output, and effectiveness, and made it easier to take in, indicating that it could be a viable substitute (Kim & Park, 2022).

Design and Optimization of Lornoxicam Dispersible Tablets

One study was performed to implement the Quality by Design methodology for optimization of the formulation of lornoxicam tablets; dispersible.(Almotairi et al., 2022) To assess the impact of critical variables Box–Behnken design was used such as filler ratio, concentration of disintegrant, and time of mixing, and on significant quality attributes such as friability, dissolving efficiency, and dispersibility time (Almotairi et al., 2022). FTIR and DSC analysis of drug-excipient interactions revealed no meaningful chemical interactions. Enhanced stability tests showed suitable tablet characteristics. In comparison to available tablets in the market, the modified formulation demonstrated an improved dissolution profile and stability, which may provide the benefit of less gastrointestinal discomfort (Almotairi et al., 2022).

Creation of Green Micellar Using HPLC Method to Measure Amlodipine and Atorvastatin Using QBD Approach

The study presents a novel approach that combines QbD with analytical chemistry to quantify amlodipine and atorvastatin in pharmaceuticals simultaneously (Habib et al., 2020). In keeping with green principles, micellar liquid chromatography is employed to reduce the amount of organic solvent utilized. Method greenness is evaluated using tools such as NEMI labeling (Habib et al., 2020). The process is methodically created, pinpointing critical parameters and optimizing conditions. Validation verifies precision and accuracy. Its applicability to commercial tablets demonstrates its usefulness. This method

combines analytical precision with ecological awareness to provide a new approach with increased greenness and sensitivity (Habib et al., 2020).

Using Quality by Design in the Development and Characterisation of Nanocarrier of Azithromycin

Using a qbd advanced method, a nanocarrier for azithromycin (AZT) with the goal of reducing side effects and improving treatment efficacy was created. Critical material attributes and Critical process parameters were identified and optimized through the application of Taguchi design and Box-Behnken Design (BBD) optimization methodologies. The nanocarrier demonstrated favorable characteristics such as stability in a wide range of environments, enhanced bioavailability, and a sustained release profile (Patil et al., 2020). This methodical approach presents a viable approach to the formulation of nanocarriers, which may improve drug delivery systems for poorly soluble medicines such as AZT and lead to better patient outcomes (Patil et al., 2020).

QbD and Risk Assessment Approach and Pharmacokinetic Profile of Fixed Dose Single Tablet Formulation along with Differential Release

To improve patient compliance, a different release of the fixed dosage tablet containing simvastatin (SIM) and amlodipine besylate (AML-B) was developed. Phase one involved determining the release regulating parameters for AML-B and SIM granules.(Kanwal et al., 2021) Phase two involved preparing and optimizing a fixed dosage formulation for a drug's differential release via the use of quality by design and techniques for risk assessment. In the third phase, the PKs of the aforementioned medications were examined in healthy dogs.(Kanwal et al., 2021) AML-B was released under control over an 8-hour period in the optimized formulation via using an Eudragit dicalcium phosphate mix; nevertheless, this controlled release of diffusion was predicated on first-order kinetics. The improved FDC tablet formulation resulted in delayed release, delaying the release of SIM by more than 8 hours after the release of AML-B (Kanwal et al., 2021). AML-B and SIM had HPLC retention durations of 2.10 and 15.52 minutes, respectively. AUCo- was reduced by twofold, however AUCo- of amlodipine-B was enhanced by three times. amlodipine-B and SIM had tmax values of 12 and six hours, respectively. The AML-B had zero lag time (lag), whereas SIM exhibited a tlag of 6.33 0.81 h, therefore fulfilling the study's purpose (Kanwal et al., 2021).

The Creation of Loaded Nanostructured Aceclofenac Lipid Carriers by Qbd Gives an Enhanced Inflammatory Dermatokinetic Profile

The goal of the previous study was to create and evaluate loaded aceclofenac nanostructured lipid carriers of aceclofenac using a methodology centered around quality by design. The stability and potential for transdermal penetration of the NLCs were assessed (Garg et al., 2017). Using Quality by Design software, loaded nanostructured aceclofenac lipid carriers were produced, described, and further assessed for transdermal absorption capability and stability. Using the microemulsion process, several lipids and mostly surfactants were selected as key material attributes (CMAs) for the preparation of NLCs. For the purpose of optimizing and assessing for several key attributes of quality, such as zeta potential, particle size, in vitro drug release, and polydispersity index, a 33 factorial design was employed. To maximize NLCs, the impact of CMAs, and surfactant conc., on quality attributes, such as particle size and efficiency of drug entrapment, was assessed (Garg et al., 2017). The refined NLCs were then added to carbopol gel and assessed both in vitro and in vivo after being described for texture and rheology profile. It was discovered that the improved ACE-NLCs had increased drug loading and entrapment efficiency and were spherical and nanometric in size. The produced formulation complied with the Fickian diffusion-demonstrating Korsmeyer-Peppas model, according to the findings of the in-vitro drug release. The drug was released in two stages, first burst release and then continuous for 48 hours. In comparison to the commercial products, the modified NLCs-based gel formulation demonstrated enhanced ex vivo permeability efficiency through the skin, superior texture, and a rheological profile. It also demonstrated improved efficiency of cell update on hyperkeratinocytic cells. Using carrageenan-induced edema mice in dermatokinetic modeling and pharmacodynamic studies, the results indicate that NLCs loaded with aceclofenac hydrogel may offer a superior delivery option for the aim of targeting different layers of skin (Garg et al., 2017).

Discussion

Qbd ideas are being applied to the development process of pharmaceuticals providing a methodical way to

guarantee reliable product quality, adherence to regulations, and better results for patients. QbD helps businesses to promote quality in their products from starting by focusing on established objectives, product and process comprehension, and risk management. Improved drug levels and bioavailability in vivo were the results of optimized formulations, indicating greater therapeutic potential. The study highlights a range of studies that demonstrate how QbD procedures improve product quality and reliability, from the creation of analytical methods to the production of nanoparticles. The composition of the mobile phase, stationary phase, and pH of the buffer are threshold parameters that have a considerable impact on technique performance. QbD successfully facilitates the achievement of targeted product features by optimizing essential quality attributes and process parameters utilizing systematic methodologies like factorial design and response surface analysis. Comprehending the features of the product and the process lowers variability, improving quality and compliance. QbD integration promotes creativity, lowers costs and risks, and complies with legal constraints in the pharmaceutical development process. Using QbD concepts in a systematic manner provides high-quality, effective products. Better skin penetration and antitumor effectiveness were demonstrated by nanoparticles. Using QbD principles, consistent product quality is ensured by real-time monitoring as well validating the method ensures that it is appropriate for use in commercial settings.

Conclusion

Our comprehensive review found that qbd was used in the past for the manufacturing of various pharmaceutical products and by considering the quality attributes of the formulations and processes it resulted in the production of top-notch products with minimum utilization of resources and it lowered cost and risks by preliminary drug designs.

The significance of qbd in the creation of pharmaceutical formulations is highlighted by this research. While adhering to regulatory requirements, QbD principles enable systematic optimization, guarantee product quality, and improve therapeutic efficacy. Developing stable, efficient, and novel medication formulations requires the combination of experimental designs, risk assessments, and real-time monitoring.

References

Almotairi, N., Mahrous, G. M., Al-Suwayeh, S., & Kazi, M. (2022). Design and optimization of Lornoxicam Dispersible Tablets using the Quality by Design (QBD) approach. *Pharmaceuticals*, *15*(12), 1463. https://doi.org/10.3390/ph15121463
Google Scholar Worldcat Fulltext

Amasya, G., Aksu, B., Badilli, U., Onay-Besikci, A., & Tarimci, N. (2019). QbD guided early pharmaceutical development study: Production of lipid nanoparticles by high pressure homogenization for skin cancer treatment. *International Journal of Pharmaceutics*, *563*, 110–121. https://doi.org/10.1016/j.ijpharm.2019.03.056
Google Scholar Worldcat Fulltext

Beg, S., Hasnain, M. S., Rahman, M., & Swain, S. (2019). Introduction to Quality by Design (QBD): fundamentals, principles, and applications. In *Elsevier eBooks* (pp. 1–17). https://doi.org/10.1016/b978-0-12-815799-2.00001-0
Google Scholar Worldcat Fulltext

Bhusnure, O., Nandgave, A., Gholve, S. B., Thonte, S. S., Shinde, C. A., & Shinde, N. (2015). Formulation and evaluation of fast dissolving tablet on montelukast sodium by using QbD approach. *Indo Am J Pharm Sci*, *5*, 1092.
Google Scholar Worldcat Fulltext

Garg, N. K., Sharma, G., Singh, B., Nirbhavane, P., Tyagi, R. K., Shukla, R., & Katare, O. (2017). Quality by Design (QbD)-enabled development of aceclofenac loaded-nano structured lipid carriers (NLCs): An improved dermatokinetic profile for inflammatory disorder(s). *International Journal of Pharmaceutics*, *517*(1–2), 413–431. https://doi.org/10.1016/j.ijpharm.2016.12.010
Google Scholar Worldcat Fulltext

Grangeia, H. B., Silva, C., Simões, S. P., & Reis, M. S. (2020). Quality by design in pharmaceutical manufacturing: A systematic review of current status, challenges and future perspectives. *European Journal of Pharmaceutics and Biopharmaceutics*, *147*, 19–37. https://doi.org/10.1016/j.ejpb.2019.12.007
Google Scholar Worldcat Fulltext

Gurumukhi, V. C., & Bari, S. B. (2020). Fabrication of efavirenz loaded nano-formulation using quality by design (QbD) based approach: Exploring characterizations and in vivo safety. *Journal of Drug Delivery Science and Technology*, *56*, 101545. https://doi.org/10.1016/j.jddst.2020.101545
Google Scholar Worldcat Fulltext

Habib, A. A., Hammad, S. F., Megahed, S. M., & Kamal, A. H. (2020). Innovative Quality by Design approach for development of Green Micellar HPLC method for simultaneous determination of atorvastatin and amlodipine. *Chromatographia*, *83*(10), 1221–1231. https://doi.org/10.1007/s10337-020-03937-5
Google Scholar Worldcat Fulltext

Kanwal, U., Mukhtar, S., Waheed, M., Mehreen, A., Abbas, N., Shamim, R., Hussain, K., Rasool, F., Hussain, A., & Bukhari, N. I. (2021). Fixed Dose Single Tablet Formulation with Differential Release of Amlodipine Besylate and Simvastatin and Its Pharmacokinetic Profile: QbD and Risk Assessment Approach. *Drug Design, Development and Therapy*, *Volume 15*, 2193–2210. https://doi.org/10.2147/dddt.s240506
Google Scholar Worldcat Fulltext

Kim, J., & Park, Y. (2022). QbD Consideration for Developing a Double-Layered Tablet into a Single-Layered Tablet with Telmisartan and Amlodipine. *Pharmaceutics*, *14*(2), 377. https://doi.org/10.3390/pharmaceutics14020377
Google Scholar Worldcat Fulltext

Yu, L. X., Amidon, G., Khan, M. A., Hoag, S. W., Polli, J., Raju, G. K., & Woodcock, J. (2014). Understanding pharmaceutical quality by design. *the œAAPS Journal*, *16*(4), 771–783. https://doi.org/10.1208/s12248-014-9598-3
Google Scholar Worldcat Fulltext

Mishra, V., Thakur, S., Patil, A., & Shukla, A. (2018). Quality by design (QbD) approaches in current pharmaceutical set-up. *Expert Opinion on Drug Delivery*, *15*(8), 737–758. https://doi.org/10.1080/17425247.2018.1504768
Google Scholar Worldcat Fulltext

Park, S. Y., Kang, Z., Thapa, P., Jin, Y. S., Park, J. W., Lim, H. J., Lee, J. Y., Lee, S., Seo, M., Kim, M., & Jeong, S. H. (2019). Development of sorafenib loaded nanoparticles to improve oral bioavailability using a quality by design approach. *International Journal of Pharmaceutics*, *566*, 229–238. https://doi.org/10.1016/j.ijpharm.2019.05.064
Google Scholar Worldcat Fulltext

Patel, K. Y., Dedania, Z. R., Dedania, R. R., & Patel, U. (2021). QbD approach to HPLC method development and validation of ceftriaxone sodium. *Future Journal of Pharmaceutical Sciences*, *7*(1). https://doi.org/10.1186/s43094-021-00286-4
Google Scholar Worldcat Fulltext

Patil, A. S., & Pethe, A. M. (2013). Quality by Design (QbD) : A new concept for development of quality pharmaceuticals. *International Journal of Pharmaceutical Quality Assurance, 4(2), 13-19.*, *4*(02), 13–19. https://doi.org/10.25258/ijpqa.4.2.1
Google Scholar Worldcat Fulltext

Patil, S., Gattani, S., Nirbhavane, P., Katare, O., & Patil, K. (2020). Quality by design-enabled development and characterisation of nanocarrier of azithromycin. *Current Medicine Research and Practice*, *10*(6), 272. https://doi.org/10.4103/cmrp.cmrp_43_20
Google Scholar Worldcat Fulltext

Prasad, P. S., Imam, S. S., Aqil, M., Sultana, Y., & Ali, A. (2014). QbD-based carbopol transgel formulation: characterization, pharmacokinetic assessment and therapeutic efficacy in diabetes. *Drug Delivery*, *23*(3), 1047–1056. https://doi.org/10.3109/10717544.2014.936536
Google Scholar Worldcat Fulltext

Zhang, L., & Mao, S. (2017). Application of quality by design in the current drug development. *Asian Journal of Pharmaceutical Sciences*, *12*(1), 1–8. https://doi.org/10.1016/j.ajps.2016.07.006
Google Scholar Worldcat Fulltext