

**RESEARCH ARTICLE**

## **Formulation Development and Characterization of Darunavir and Ritonavir Immediate Release Tablets using Quality by Design approach**

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**ABSTRACT:**

Darunavir is a nonpeptidic inhibitor of protease and is primarily metabolized by cytochrome P450 3A (CYP3A) isoenzymes. It is usually Co-administered with low-dose ritonavir (Darunavir/r). Ritonavir is an inhibitor of CYP3A isoenzymes and pharmacologically enhances Darunavir which leads to increased plasma concentrations of darunavir and allows for daily lower dose. Here, we have developed combination IR formulation of Darunavir and Ritonavir and evaluated. In vitro drug release of all formulations was carried out in dissolution medium 900ml of pH 3.0 0.05 M Sodium Phosphate Buffer + 2% Tween 20 for 75 Min USP II apparatus (paddle). The results shown that, all the formulations of matrix tablets shown the good release of drug from trialed formulations however all formulations were not releasing the drug in enough amount. In matrix tablets F8, the release of drug shows 99%. So, the formulation F8 has been considered as suitable for the immediate release of Darunavir and Ritonavir. Tablets were also evaluated for physico-chemical properties, dissolution studies and through Quality by Design (QbD) method.

**KEYWORDS:** Darunavir, Ritonavir, Immediate release tablet, Dissolution, Quality by design.

**INTRODUCTION:**

For each disease condition or the disorder state of the patient, appropriate treatment is very important to maintain good health of the patient. For the same, the drug is administered conventionally by one or more of several well defined and popular routes of drug administration which include but not limited to oral, parenteral, rectal, alveolar, ocular and topical etc.<sup>1, 20</sup> As per current scenario, conventional dosage forms of drugs are being replaced by the novel drug delivery systems. Drugs with matrix system structure is the dosage system which is used to prolong the drug effect and also controls the drug release which is being dissolved or dispersed.<sup>2</sup> Before 1950, most of the drugs were formulated in pills or capsules formulation and that released the loaded drug immediately upon contact with water without any ability to control the drug release kinetics. In 1952, Smith Klein Beecham introduced the first immediate release formulation that was able to control the drug release kinetics and achieve 12-hour efficacy.<sup>3</sup>

Over the past 30 years, as the expense and complications involved in marketing new drug entities have increased with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention has been focused on development of immediate or controlled-release drug delivery systems.<sup>4,7</sup> Oral route of drug delivery system is considered to be convenient and safe due to its ease of administration, patient acceptance and cost effective manufacturing process.<sup>4,5,6,9,10</sup> In recently era, many technical advancements have been done resulting in the development of new techniques for drug delivery. These techniques are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and/or targeting the delivery of drug to a tissue i.e. targeted drug delivery system. The most important objective for the development of these systems is to furnish an extended duration of action and thus assure greater patient compliance.<sup>11-19</sup>

The goal in designing immediate drug delivery systems is to facilitate patients for ease of patient compliance. Also to check the immediate release behavior of tablet as well as the physical and chemical stability of the product.<sup>9</sup> Immediate release formulation is dose multiple



## **Development and Validation of a New RP-HPLC Analytical Method for the Simultaneous Determination of Luliconazole and Clobetasol Propionate in Synthetic Mixture**

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### **Authors' contributions**

*This work was carried out in collaboration with both authors. Author BS designed the study, performed the statistical analysis and wrote the first draft of the manuscript. Author HJ managed the analyses of the study, guided the entire research work and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i32B31742

#### Editor(s):

(1) Dr. Q. Ping Dou, Barbara Ann Karmanos Cancer Institute, Wayne State University, USA.

(2) Dr. Ana Cláudia Coelho, University of Trás-os-Montes and Alto Douro, Portugal.

#### Reviewers:

(1) Vandana Jain, Oriental College of Pharmacy, India.

(2) Ramreddy Godela, Bhaskar Pharmacy College, India.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/69348>

**Original Research Article**

**Received 06 April 2021**

**Accepted 11 June 2021**

**Published 21 June 2021**

### **ABSTRACT**

**Aim:** To develop new selective and sensitive reverse-phase high-performance liquid chromatography (RP-HPLC) approach for the quantification of antifungal drug Luliconazole integrate with corticosteroid drug Clobetasol Propionate in a synthetic mixture.

**Methods:** The method was validated to achieve International Conference Harmonization (ICH) requirements. Chromatographic separation was carried out by isocratic technique on a reversed-phase Inertsil C18 column (5  $\mu$ m, 250mm x 4.6mm i.d with the mixture of Acetonitrile: Water pH adjusted with H<sub>3</sub>PO<sub>4</sub> (60: 40) and UV detection at 264 nm. The compounds were eluted at a flow rate of 1.0 mL/min with an injection volume of 20 $\mu$ L.

**Results:** The calibration curves were linear ( $r^2 > 0.999$ ) over the concentration range 10-200  $\mu$ g/mL for Luliconazole and 5-100  $\mu$ g/mL for Clobetasol Propionate. The average retention times for Luliconazole and Clobetasol Propionate were 3.16 and 6.94 min, respectively. The % RSD for the

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# Development of Interpenetrating Microspheres of Chitosan and Gum Arabic for Epigallocatechin Gallate to Enhance Colonic Delivery

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Patel *et al.*: Development of Epigallocatechin Gallate microspheres for colon

Epigallocatechin gallate is a potent phytochemical with wide biological activity and is a class III drug. The therapeutic effect is limited, owing to poor stability and limited membrane permeability across the intestine. The aim of this study was to develop and evaluate colon-targeted microspheres of epigallocatechin gallate, using natural polymers. Water-in-oil emulsion crosslinking technique was used to prepare microspheres of epigallocatechin gallate using interpenetrating network of chitosan and gum acacia and glutaraldehyde was used as a crosslinking agent. Prepared microspheres were filled in capsules coated with Eudragit S100. The prepared microspheres were evaluated *in vitro* for preformulation studies, encapsulation efficiency, micromeritic properties, dissolution studies and stability studies. Fourier transform infrared spectroscopy and differential scanning calorimetry studies had proved that the drug and polymers are compatible. The good flow property of microspheres show that the microspheres are not aggregated. Scanning electron microscope micrographs of microspheres show a rough and folded surface morphology. The microspheres are spherical and uniform in shape. Formulations show good encapsulation efficiency. Formulation F1 to F6 show sustained release of drug for 10 h. The *in vitro* drug release of batch F1 to F6 were best explained by Higuchi models due to diffusion mechanism of drug release from polymeric matrix system. The selected formulation batch for a period of 3 mo at  $40 \pm 2^\circ/75 \pm 5\%$  RH show no significant changes. The current approach was helpful to develop polysaccharide based microspheres of epigallocatechin gallate to enhance colonic drug delivery.

**Key words:** Epigallocatechin gallate, gum arabic, chitosan, colonic drug delivery, microspheres

Extensive research has expanded the role of green tea as bioactive molecules from a traditional beverage for healing many health ailments. *Camellia sinensis* is ample with catechins consisting of around 8 polyphenolic compounds. Different sources suggest, the most plentiful catechins present in tea are (-)-epigallocatechin gallate (EGCG) and (-)-epigallocatechin (EGC)<sup>[1,2]</sup>. EGCG shows beneficial health effects including anti-oxidation<sup>[3]</sup>, anti-diabetes<sup>[4]</sup>, anti-inflammation<sup>[5,6]</sup> and anti-tumorigenesis activity<sup>[7]</sup>.

Many possible mechanisms have been explored to study the healthy benefits of tea catechins, in various areas such as antioxidative activity, regulating the tumor-suppressor microRNAs, inhibiting C-Met (hepatocyte growth factor receptor (HGFR)) activity, inhibiting I $\kappa$ B kinase activity<sup>[3,8-11]</sup>. The preventive

actions of EGCG on signaling pathways controlling cyclooxygenase 2 (COX-2) expressions were observed. EGCG suppressed the extracellular signal-regulated protein kinase (ERK1/2) and Protein kinase B (PKB/Akt) pathways in colon cancer cells<sup>[12]</sup>.

However, the oral administration of green tea catechins shows sub-or low-micromolar range peak plasma levels in human subjects or animals<sup>[13,14]</sup>, which was lesser compared to the effective concentration of *in vitro* tests. Therefore, the practical utility of this therapeutically

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## **Implementation of QbD Principles for Simultaneous Quantitative Expression of Olmesartan Medoxomil, Telmisartan and Hydrochlorothiazide by RP-HPLC**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author BM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors HJ and US managed the analyses of the study. Author PP managed the literature searches. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i41A32301

*Editor(s):*

(1) Dr. Jongwha Chang, University of Texas, College of Pharmacy, USA.

*Reviewers:*

(1) K. Priya, SRM Institute of Science & Technology, India.

(2) Khadiga Mohamed Ahmed, National Research Centre, Egypt.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/72363>

**Original Research Article**

**Received 05 June 2021**  
**Accepted 10 August 2021**  
**Published 14 August 2021**

### **ABSTRACT**

**Aim and Study Design: Aims:** The current research paper describes the RP-HPLC Method for estimation of Olmesartan Medoxomil, Telmisartan, and Hydrochlorothiazide and implements the role of QbD for Data Analysis

**Study design:** Mentioned study is simple, rapid, economical, accurate, and robust RP-HPLC Method for Olmesartan Medoxomil, Telmisartan, and Hydrochlorothiazide and implementing QbD Approach for Data Analysis.

**Place and Duration of Study:** The present study was carried out at Smt. S. M. Shah Pharmacy College, Mahemdabad, Gujarat, India from October 2019 to February 2020.

**Methodology:** The separation was done on Hypersil ODS C18 column with dimensions (250mm x 4.6ID, Particle size: 5 microns) and Methanol: 0.02M potassium dihydrogen phosphate buffer (60:40%v/v) pH 3 used as mobile phase. The flow rate was 1.2ml/min; detection at 254nm. QbD

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# Optimization of Amorphous Solid Dispersion Techniques to Enhance Solubility of Febuxostat

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**Received:** 1 July 2020 ♦ **Accepted:** 4 Sep 2020 ♦ **Published:** 31 Aug 2021

**Citation:** Patel VP, Patel AP, Shah A. Optimization of amorphous solid dispersion techniques to enhance solubility of febuxostat. Folia Med (Plovdiv) 2021;63(4):557-68. doi: 10.3897/folmed.63.e55838.

## Abstract

Febuxostat is a selective inhibitor of xanthine oxidase and belongs to BCS class II drugs having low solubility and high permeability. Solubility is the most important parameter which directly affects dissolution, absorption and bioavailability of the drugs. There are different techniques by which we can improve solubility and dissolution rate of poorly soluble drug. Amorphous solid dispersion is one of the methods which can improve solubility as well as powder characteristics. The aim of the present study was to formulate and optimize various methods of formulating solid dispersion by using various drug-to-polymer ratios and identifying the batch which gives higher solubility as well as amorphous powder of the drug febuxostat. Different techniques like hot melt method, solvent evaporation method and spray drying techniques were selected for optimization. Attempts were made to improve solubility of febuxostat by employing Kolliphor P 188, Kolliphor P 237, Eudragit RLPO in different drug-to-polymer ratios (1:1, 1:1.5, 1:2) as carrier. The prepared solid dispersion was characterized for the saturation solubility, percentage yield, using differential scanning calorimetry (DSC), scanning electron microscopy (SEM), powdered X-ray diffraction studies (PXRD), and residual solvent determination. Solid state characterization indicated that febuxostat was present in the amorphous form after mixing with polymeric carrier. In contrast to the pure form of drug, solid dispersion of the drug showed better solubility and amorphous characteristics which can be attributed to decreased crystallinity due to hydrotrophy. Thus, amorphous solid dispersion approach can be used successfully to enhance solubility, dissolution rate and bioavailability of febuxostat.

## Keywords

febuxostat, Kolliphor P237, solid dispersion, solubility, spray drying method

## INTRODUCTION

Over the years, the majority of compounds have been supplied as a crystalline form due to the high chemical stability, purity and relatively tight packing of molecules in its crystal lattice. Active pharmaceutical ingredient (API) should have sufficient amount of aqueous solubility to dissolve completely in the dissolution media and lipophilicity to pass across the biological membrane.<sup>1</sup> According to

the biopharmaceutical classification system (BCS), class II and IV drugs possess low aqueous solubility and high membrane permeability. Therefore, drugs of these classes face problems during aqueous dissolution in various manufacturing processes. This hydrophobicity of the drug can be improved by changing the various physicochemical properties of the drug.<sup>2</sup> Low aqueous solubility of API can be improved by adding surfactants, solubility enhancers, complexing agents, cyclodextrins and forming supersaturated solution of the drug.

ISSN 0974-3618 (Print)  
0974-360X (Online)

www.rjptonline.org



## RESEARCH ARTICLE

# Formulation and Evaluation of Benidipine Nanosuspension

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### ABSTRACT:

In the interest of administration of dosage form oral route is most desirable and preferred method. After oral administration to get maximum therapeutic effect, major challenge is their water solubility. Water insoluble drug indicate insufficient bioavailability as well dissolution resulting in fluctuating plasma level. Benidipine (BND) is poorly water soluble antihypertensive drug has lower bioavailability. To improve bioavailability of Benidipine HCL, BND nanosuspension was formulated using media milling technique. HPMC E5 was used to stabilize nanosuspension. The effect of different important process parameters e.g. selection of polymer concentration  $X_1$  (1.25 mg), stirring time  $X_2$  (800 rpm), selection of zirconium beads size  $X_3$  (0.4mm) were investigated by  $2^3$  factorial design to accomplish desired particle size and saturation solubility. The optimized batch had 408 nm particle size  $Y_1$ , and showed *in-vitro* dissolution  $Y_2$   $95 \pm 0.26$  % in 30 mins and Zeta potential was -19.6. Differential scanning calorimetry (DSC) and FT-IR analysis was done to confirm there was no interaction between drug and polymer.

**KEYWORDS:** Benidipine, Bioavailability, Nanosuspension, Factorial design, Media milling, Solubility.

### INTRODUCTION:

Drugs with poor aqueous solubility are increasingly posing challenges in the development of new drugs, since more numbers of poorly water-soluble drugs are introduced in the pharmaceutical era<sup>1</sup>. Bioavailability of drug depends on its solubility and permeability as well dissolution in a medium<sup>2</sup>. Bioavailability is a crucial challenge to the therapeutic efficacy of a drug regarding its route of administration<sup>3</sup>. Dissolution involves the process of transfer of solid drug particles into solution in the surrounding physiological fluid. The low aqueous solubility of Biopharmaceutics Classification System (BCS) class II drugs is a major issue for their clinical application<sup>4</sup>. To overcome this major obstacle some conventional methods such as micronization, chemical modification, solid dispersion, liposomes<sup>5</sup>, salt formation, pH adjustments, cyclodextrin complexation<sup>6</sup>, mucoadhesive microspheres, nanoparticles, nanosuspensions, micro emulsion<sup>7,8</sup>, and self emulsifying systems are available to enhance the solubility,

Dissolution rate and bioavailability of poorly soluble BCS Class II drugs, whereby the drug is formulated and maintained as nano size drug particle which are then suspended in a liquid usually water to form nanosuspensions<sup>9</sup>. Nanosuspensions have become a popular approach to improve the solubility. Nanosuspensions can be formulated either by particle size reduction of large drug particles to nanosized as top-down approach or by the precipitation of dissolved molecules into crystals as bottom up approach<sup>10</sup>. In media milling technique, top down approach, for the mechanical grinding of drug, zirconium beads and stabilizer was used to obtain nanosuspensions. Compared to other nano sizing techniques, media milling avoids organic solvents and is easy to scale up. For the formulation of nanosuspension polymers can be used like polyvinylpyrrolidone K30 (PVP K30), Poloxamer 188, Tween 80, Tween 20, HPMC E5, HPMC E15. BND is a dihydropyridine-derived calcium channel blocker having different mechanisms of action, that is, triple calcium channels (L, N, and T) blocking action. BND has relatively high vascular selectivity. The oral administration of BND is rapidly absorbed. But a dose of 8mg of BND in the fed state delay the rate of absorption and an increase in the area under the concentration curve when compared with the fasting state has been observed.

Received on 04.08.2020      Modified on 17.09.2020  
Accepted on 19.10.2020      © RJPT All right reserved  
Research J. Pharm. and Tech. 2021; 14(8):4111-4116.  
DOI: 10.52711/0974-360X.2021.00712

# Structural and biological aspects of natural bridged macrobicyclic peptides from marine resources

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## Abstract

Among peptide-based drugs, naturally occurring bicyclic compounds have been established as molecules with unique therapeutic potential. The diverse pharmacological activities associated with bicyclic peptides from marine tunicates, sponges, and bacteria render them suitable to be employed as effective surrogate between complex and small therapeutic moieties. Bicyclic peptides possess greater conformational rigidity and higher metabolic stability as compared with linear and monocyclic peptides. The antibody-like affinity and specificity of bicyclic peptides enable their binding to the challenging drug targets. Bridged macrobicyclic peptides from natural marine resources represent an underexplored class of molecules that provides promising platforms for drug development owing to their biocompatibility, similarity, and chemical diversity to proteins. The present review explores major marine-derived bicyclic peptides including disulfide-bridged, histidinotyrosine-bridged, or histidinoalanine-bridged macrobicyclic peptides along with their structural characteristics, synthesis, structure–activity relationship, and bioproperties. The comparison of these macrobicyclic congeners with



## Research article

## Analytical method development and validation of related substances by rp-hplc of emtricitabine and tenofovir disoproxil fumarate tablets

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**ABSTRACT**

The developed method was a simple, accurate, precise, specific and robust method for the validation of Emtricitabine and Tenofovir Disoproxil Fumarate Tablets by reverse phase high pressure liquid chromatography. For Emtricitabine and Tenofovir Disoproxil Fumarate Chromatography was performed on Agilent 1200 series, UV and PDA Detector, Waters X-bridge C18 (250 mm x 4.6 mm, 5  $\mu$ m) by preparing Buffer solution: Dissolve 0.63 g of ammonium formate in 1000 mL of purified water and mix. Adjust to pH of 3.90  $\pm$  0.05 with diluted formic acid. And used it as mobile phase A. Mobile Phase B: mixture of buffer solution and methanol in the ratio of (20 : 80) % v/v at a flow rate of 1.0 mL/min and at 254 nm wavelength. The retention times of Emtricitabine and Tenofovir Disoproxil Fumarate are approx. 29 min and 70 min. respectively. 5-Fluorocytosine, Sulfoxide Impurity Isomer 1, Sulfoxide Impurity isomer 2, 5-Fluorouracil analogue, Tenofovir (PMPA) Impurity, Monoester Impurity and Dimer Impurity found linear over the range of LOQ - 150 % of target concentration. Method also found precise by spiking impurities at specification level. Accuracy was demonstrated at LOQ - 150 % level by preparing sample in triplicate for each level and found accurate. Hence, the method could be successfully used for the analysis of impurities in Emtricitabine and Tenofovir Disoproxil Fumarate Tablets.

**Keywords:** Emtricitabine, Tenofovir Disoproxil Fumarate, HPLC, UV and PDA Detector, Related Substances.

Received - 04-06-2021, Reviewed - 07/07/2021, Revised/ Accepted- 03/09/2021

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**INTRODUCTION**

In the Era of Sciences and medical, Pharmaceutical industries are playing the vital role worldwide. Now a day's humans are suffering from many critical diseases however to overcome this pharmaceutical industries are producing innovating new chemical entities. Regulatory bodies like USFDA, TGA, MHRA, WHO etc. have certain guidelines to make qualitative and effective medicines. To fulfill requirement and produce qualitative medicine analytical part also play a vital role and now a day's industries are highly focusing on it [1].

Several reasons are available for the development of a new method of analysis, they are

- There may not a suitable method for a particular analyte in the sample matrix.
- Existing may be too erroneous.
- Existing method may not provide adequate sensitivity.
- Existing methods are too expensive and time consuming [2].

Antiviral drugs are a class of medication used specifically for treating viral infections rather than bacterial ones. Most antiviral

are used for specific viral infections, while a broad-spectrum antiviral is effective against a wide range of viruses. Unlike most antibiotics, antiviral drugs do not destroy their target pathogen; instead they inhibit their development [3].

**MATERIAL AND METHOD DEVELOPMENT****Instruments used**

Table 1: Instrument Used during Development

Name	Make/Model
HPLC	Agilent
Series	1200, 1260
Software	Chromeleon
Pump	Isocratic
Column	Waters X-bridge C18 (250 mm x 4.6 mm, 5 $\mu$ m)
Detector	UV Detector PDA Detector

**Reagents used**

Ammonium formate (LCMS grade), Formic acid 99% (HPLC grade), Water (Milli Q grade) and Methanol (Gradient grade).

**PREPARATION OF SOLUTIONS****Preparation of Diluent**

Prepare a mixture of purified water and methanol in the ratio of (80:20) % v/v.





## **Development, Validation and Forced Degradation Study of Emtricitabine and Tenofovir Alafenamide in its Pharmaceutical Dosage Form Using RP-HPLC**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author KP designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors US and HJ managed the analyses of the study. Authors JKP and TBP managed the literature searches. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i43A32462

Editor(s):

(1) Rafik Karaman Al-Quds University Medical School, Palestine.

Reviewers:

(1) Naveen Kumar, Lady Hardinge Medical College and Associated Hospital, India.

(2) Pattana Sripalakit, Naresuan University, Thailand.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/73176>

**Original Research Article**

**Received 26 June 2021  
Accepted 01 September 2021  
Published 03 September 2021**

### **ABSTRACT**

**Aims:** The present research was aimed to develop and validate a reverse phase high performance liquid chromatographic (RP-HPLC) method for the quantification of Emtricitabine (EMT) and Tenofovir Alafenamide (TEN) in combination.

**Methodology:** Separation was achieved under optimized chromatographic condition on an Inertsil C18, 250 x 4.6 mm, 5 $\mu$ m column. Various composition of mobile phase was tried. Separation of EMT and TEN was started with Methanol: Buffer and Methanol finally using solvent system of Buffer (pH 3.5) and Methanol in ratio of (30:70) and flow rate adjust at 1.0 ml/min was used as solvent system, the detection was carried out at 262nm using Shimadzu UV-visible detector. The mobile phase run time for the developed analytical method was 10 minutes.

**Results:** The standard curve was found linear in the concentration range of 20-60  $\mu$ g/ ml ( $r^2$ -0.9994) and 2.5-7.5  $\mu$ g/ ml ( $r^2$ -0.9992) for EMT and TEN respectively. The %RSD was found to be 0.80-0.95% and 0.63-1.09 for EMT and TEN respectively. Percentage (%) recoveries for EMT and

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## **“Robust and Rapid” UV Spectroscopic Method for Estimation of Luliconazole and Clobetasol Propionate Drug Combination**

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*This work was carried out in collaboration between both authors. Author BS designed the study, performed the statistical analysis and wrote the first draft of the manuscript. Author HJ managed the analyses of the study, guided the entire research work. Both authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i45A32748

#### Editor(s):

(1) Dr. Sawadogo Wantinga Richard, Ministry of Higher Education, Scientific Research and Innovation, Burkina Faso.

(2) Dr. Farzaneh Mohamadpour, University of Sistan and Baluchestan, Iran.

#### Reviewers:

(1) Nohad Alomari, Knowledge University, Iraq.

(2) Jyothi Penta, HITS College of Pharmacy, India.

Complete Peer review History: <https://www.sdiarticle4.com/review-history/74511>

**Original Research Article**

**Received 15 July 2021**

**Accepted 25 September 2021**

**Published 01 October 2021**

### **ABSTRACT**

**Objective:** The new combination for Luliconazole and Clobetasol Propionate was approved for the treatment of variety of skin disease. The main objective of this research is development and validation of novel, simple, fast and responsive derivative spectroscopic process for simultaneous estimation of newly approved combination Luliconazole (LLZ) and Clobetasol Propionate (CLP).

**Methodology:** Here in this first derivative spectroscopic method, the absorbance of LLZ and CLP was taken at 312nm (ZCP of CLP) and 249nm (ZCP of LLZ) respectively. Establishment of linearity was in a concentration varies from 10-50 µg/ml for Luliconazole and 5-25µg/ml for Clobetasol Propionate.

**Results:** From the method developed above the R<sup>2</sup> value observed for LLZ and CLP is 0.9988 and 0.9961. Statistical validation of accuracy and reproducibility was done for planned procedure with the help of recovery studies. The mean % recovery of Luliconazole and Clobetasol Propionate was

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ISSN 0974-3618 (Print)  
0974-360X (Online)

www.rjptonline.org



## **RESEARCH ARTICLE**

# **Preparation and Characterization of Curcumin and Epigallocatechin gallate co-loaded polymeric microspheres for Colonic delivery**

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### **ABSTRACT:**

Curcumin (CURC) is a natural polyphenolic compound obtained from *Curcuma longa* which shows preventive and therapeutic actions against cancer. Epigallocatechin gallate (EGCG) is a potent phytochemical obtained from *Camellia sinensis*, with wide biological activity. The therapeutic effect is limited, owing to poor stability and limited membrane permeability across the intestine. The aim of this study was to develop and evaluate colon-targeted microspheres of CURC and EGCG, using natural polymers. W/O emulsion crosslinking technique was used to prepare microspheres of CURC and EGCG using interpenetrating network (IPN) of Chitosan (CS) and Gum acacia (GA) and glutaraldehyde was used as a crosslinking agent. Prepared microspheres were filled in capsules coated with Eudragit S100. The prepared microspheres were evaluated *in vitro* for preformulation studies, encapsulation efficiency, micromeritic properties, dissolution studies and stability studies. FTIR and DSC studies had proved that the drug and polymers are compatible. The good flow property of microspheres showed that the microspheres are not aggregated. SEM micrographs of microspheres show a rough and folded surface morphology. The microspheres are spherical and uniform in shape. Formulations showed good encapsulation efficiency. Formulation F1 to F6 showed sustained release of drug for 10 h. The *in-vitro* drug release of batches was best explained by Higuchi models showing anomalous diffusion mechanism. The coated batch showed better release results. The optimized formulation for a period of 3 month at 40±2°/75 ± 5% RH showed no significant changes. The current approach was helpful to develop polysaccharide based microspheres of CURC and EGCG to enhance colonic drug delivery.

**KEYWORDS:** Curcumin, Epigallocatechin Gallate, Biodegradable polymers, Colonic drug delivery, microspheres.

### **INTRODUCTION**

Curcumin (CURC) is a principal curcuminoid (polyphenol) obtained from plant *Curcuma longa*. It is utilised as spice, colouring agent and flavouring agent<sup>1</sup>. Curcumin is known for its anticancer, anti-inflammatory, antibacterial and antioxidant activities<sup>2</sup>. These reports emphasise the capability of curcumin in overcoming multidrug resistant cancer, suppress colonic cancer, prostatic cancer, ovarian cancer and breast cancer<sup>3</sup>.

But due to its low solubility in aqueous media and less bioavailability, the practical utility of this therapeutically potential molecule is restricted<sup>4</sup>.

Cyclodextrins (CDs) are cyclic oligosaccharides which are used as solubilising and stabilising agents for lipophilic substances in aqueous preparations. They are widely used for solubility enhancement of poorly soluble drugs<sup>5,6</sup>.

Extensive research has expanded the role of green tea as bioactive molecules from a traditional beverage for healing many health ailments. *Camellia sinensis* is ample with catechins consisting of around eight polyphenolic compounds. Different sources suggest, the most plentiful catechins present in tea are (-)-epigallocatechin



## Review Article

# Surface architected metal organic frameworks-based biosensor for ultrasensitive detection of uric acid: Recent advancement and future perspectives

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## ARTICLE INFO

## Keywords:

Gout, uric acid  
Metal-organic framework  
Electrochemical biosensor  
Fluorescent biosensor  
Colorimetric biosensor

## ABSTRACT

Gout is the world's most popular inflammatory arthritis and the prevalence of gout is rapidly rising worldwide. Typically, gout develops in a single joint as excessive swelling and intense pain wherein excessive deposition of uric acid (UA) crystals results in inflammation of the joint. Accordingly, UA is considered an effective biomarker to diagnose gout. Recently, the use of innovative sensors has attracted great attention, as it is effortless, responsive, quick, and powerful. While the traditional sensors for UA assessment are widely used, they pose many limitations and hurdles in terms of sensitivity, selectivity, and simplicity. In this vein, metal ions and organic ligand-based metal-organic framework (MOF) have gained much attention for the recognition of UA due to its larger surface area, porosity, high sensitivity, and defined selectivity. In this review, we provide details on the latest developments of MOF-centered biosensors for sensitive detection of UA. The status of gout, fundamentals of MOF, and MOF availed for detection of UA have been elaborated. Besides, we highlighted the nanoparticles and conjugates that rely on advanced strategies along with MOF that boost the sensitivity and selectivity towards the UA. Interestingly, different surface architected MOFs biosensors showed a lower detection limit for UA from  $\mu\text{M}$  to  $\text{nM}$ . Finally, the threats and potential opportunities for MOF-based UA biosensors have been summarized. Therefore, based on ongoing research, the commercialization of this advanced platform for the biosensing of diverse biomarkers will open a new door for the *in vitro* diagnosis of assorted diseases.

## 1. Introduction

From its inception, arthritis is a severe health issue of a joint in almost all developed and developing nations. Arthritis is a term that derives from the Greek word "disease of the joint." Commonly, it can be stated as acute inflammation or chronic inflammation of the joint that is

sometimes with the effect of pain and sometimes co-exists with structural damage [1]. As many as 100 classes of arthritis have been characterized according to the research. Generally, it can be classified into two type's namely non-inflammatory arthritis and inflammatory arthritis. In the first category, non-inflammatory arthritis is commonly known as osteoarthritis, while inflammatory arthritis is categorized

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## **A Stability Indicating RP-HPLC Method Validation for Simultaneous estimation of Metformin HCl and Canagliflozin in Pharmaceutical Dosage Form**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author DP designed the study, wrote the protocol, performed statistical analysis and wrote first draft of manuscript. Authors US and HJ managed the final review and analysis of data. Authors JP, DP and PP managed the literature search. All authors read and approved final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i56A33901

### **Open Peer Review History:**

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/79100>

**Original Research Article**

**Received 06 October 2021**  
**Accepted 13 December 2021**  
**Published 13 December 2021**

### **ABSTRACT**

**Aims:** Canagliflozin and Metformin HCl is a new drug combination for the treatment of Diabetes Mellitus which is one of the oldest and lethal diseases of the mankind. Aim of the research work was to develop and validate novel, rapid, sensitive, specific, robust stability indicating analytical method for the simultaneous estimation of Canagliflozin and Metformin HCl in the pharmaceutical dosage form as fixed dose formulation.

**Study Design:** Method development and validation was performed as recommended in ICH guideline "Validation of analytical procedures: Test and Methodology Q2(R1)".

**Methodology:** Method develop with chromatographic parameters as C<sub>18</sub> column (250mm×4.6 mm, 5mm particle size), HPLC system with PDA detector and mobile phase contained a mixture of Phosphate Buffer pH 5.0 and Acetonitrile (60:40 v/v). The flow rate was set to 1ml/min with responses measured at 290 nm, injection volume was 20 µl, and run time of 15 mins.

**Results:** The retention time of Metformin Hydrochloride and Canagliflozin was 5.4 min and 7.6 min

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# Formulation Development and Characterization of Darunavir and Ritonavir Sustained Release Tablets Using Quality by Design Approach

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

## **Article Information**

DOI: 10.9734/JPRI/2021/v33i53B33693

Editor(s):

(1) Dr. Takashi Ikeno, National Institute of Mental Health, National Center of Neurology and Psychiatry, Japan.

Reviewers:

(1) Md. Abul Kalam Azad, AIMST University, Malaysia.

(2) Samaa Taha Abdullah, King Abdulaziz University, Jordan.

Complete Peer review History, details of the editor(s), Reviewers and additional Reviewers are available here:

<https://www.sdiarticle5.com/review-history/77179>

**Original Research Article**

**Received 15 September 2021**

**Accepted 22 November 2021**

**Published 07 December 2021**

## **ABSTRACT**

Darunavir is a nonpeptidic inhibitor of protease and is primarily metabolized by cytochrome P450 3A (CYP3A) isoenzymes. It is usually coadministered with low-dose ritonavir (Darunavir/r). Ritonavir is an inhibitor of CYP3A isoenzymes and pharmacologically enhances Darunavir which leads to increased plasma concentrations of darunavir and allows for daily lower dose. Here, we have developed combination SR formulation of Darunavir and Ritonavir and evaluated. In vitro drug release of all formulations was carried out in dissolution medium 900ml of pH 3.0, 0.05 M Sodium Phosphate Buffer + 2% Tween 20 for 75 RPM USP II apparatus (paddle). The results shown that, all the formulations of matrix tablets shown the good release of drug from trialed formulations however all formulations were not releasing the drug in enough amount. In matrix tablets F6, the release of drug shows NLT 80%. So, the formulation F6 have been considered as suitable for the SR tablet of Darunavir and Ritonavir. Tablets were also evaluated through Quality by Design (QbD) method.

**Keywords:** *Darunavir; ritonavir; sustained release; tablet; dissolution; quality by design.*

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## **Formulation and Evaluation of Floating Sustain Release Pellets of Anti Gout Drug**

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### **Authors' contributions**

*This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i60B34952

### **Open Peer Review History:**

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/80382>

**Original Research Article**

**Received 25 October 2021**

**Accepted 26 December 2021**

**Published 27 December 2021**

## **ABSTRACT**

**Objective:** The objective of this investigation was to formulate and evaluate effervescent pellets of febuxostat to achieve sustain release effect.

**Place and Duration of Study:** APMC College of Pharmaceutical education and research, Department of Pharmaceutics, Himatnagar-383001, between June 2019 and July 2021.

**Materials and Methods:** The gastro retentive effervescent pellets of febuxostat were formulated using Sodium CMC and HPMC K4M and HPMCK15M as a sustain release polymer. Pellets were prepared by extrusion- spheronization technique using microcrystalline cellulose as spheronizing agent and sodium bicarbonate and citric acid as a gas forming agent for effervescent pellets. The pellets were characterized with respect to their floating lag time, total buoyancy time and % cumulative drug release.

**Results and Discussion:** DSC study showed that there was no change in the melting endotherm of the drug and drug-polymers mixture which means drug and polymers were compatible with each other. The optimized formulation B14 exhibits a floating lag time  $4.00 \pm 0.004$  sec. and cumulative % drug release at 12th hour  $99.58 \pm 0.02$ . Scanning electron microscopy photomicrograph revealed that the surface was rough and pellets were spherical shaped in nature.

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