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3.3.1 Number of research papers published per teacher in the Journals notified on UGC website during the last five years

CALENDER YEAR 2021

S.No.	Title of paper	Name of the author/s	Department	Name of journal	ISSN number
1	Computational Study for Identifyting Promising Therapeutic Agents of Hydroxychloroquine Analogues against SARS-CoV-2.	A.Lakshmana Rao	Pharmaceutical Chemistry	Journal of Biomolecular Structure and Dynamics.	1538-0254
2	Development and Validation of a Method for Simultaneous Estimation of Sitagliptin and Ertugliflozin in Rat Plasma by LC-MS Method.	A.Lakshmana Rao	Pharmaceutical Chemistry	Current Pharmaceutical Analysis	1875-676X
3	Design, Synthesis, Hypoglycemic Activity and Molecular Docking Studies of 3-substituted-5-[(furan-2-yl)-methylene]-thiazolidine-2,4-dione Derivatives.	K. Srikanth	Pharmaceutical Chemistry	Indian Journal of Pharmaceutical Education and Research.	0019-5464
4	Design, Synthesis, Hypoglycemic Activity and Molecular Docking Studies of 3-substituted-5-[(furan-2-yl)-methylene]-	A.Lakshmana Rao	Pharmaceutical Chemistry	Indian Journal of Pharmaceutical Education and Research.	0019-5464

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	thiazolidine-2,4-dione Derivatives.				
5	Rapid Quantitative Estimation of Metformin and Ertugliflozin in Rat Plasma by Liquid Chromatography-Tandem Mass Spectroscopy and its Application to Pharmacokinetic Studies.	A.Lakshmana Rao	Pharmaceutical Chemistry	Egyptian Pharmaceutical Journal.	2090-9853
6	Validation of a Developed Analytical Method for Determination of Nateglinide and Metformin HCl in Pure and Pharmaceutical Dosage Form by Reverse Phase High Performance Liquid Chromatography and its Degradation Studies.	A.Lakshmana Rao	Pharmaceutical Chemistry	Asian Journal of Pharmaceutical and Clinical Research. 2021:	2455-3891
7	Antidiabetic Activity of Methanolic Extract of *Searsia mysorensis* in Alloxan Induced Diabetic Rats.	A.Lakshmana Rao	Pharmaceutical Chemistry	International Journal of Pharmaceutical Sciences and Clinical Research	NA
8	Estimation of Daclatasvir in Pharmaceutical Dosge Form by Ultra Performance Liquid Chromatography.	A.Lakshmana Rao	Pharmaceutical Chemistry	International Journal of Pharmaceutical Sciences and Research.	0975-8232
9	Development of Metoprolol Tartrate Sustained Release Formulations by using Modified Starches.	A.Lakshmana Rao	Pharmaceutical Chemistry	International Journal of pharmacy &Pharmaceutical Scienc	2664-7230
10	A Review on Inductively Coupled Plasma: Mass Spectrometry with Laser Ablation.	A.Sai Datri	Pharmaceutical Analysis	Journal of Pharmaceutical and Medicinal Chemistry.	2455-8346

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11	A Review on Inductively Coupled Plasma: Mass Spectrometry with Laser Ablation.	A.Lakshmana Rao	Pharmaceutical Chemistry	Journal of Pharmaceutical and Medicinal Chemistry.	2455-8346
12	Novel RP-HPLC Method Development and Validation for Estimation of Pravastatin in Pure and Pharmaceutical Formulation.	T.Prasanthi	Pharmaceutical Analysis	Journal of Applied Pharmaceutical Sciences and Research.	2581-5520
13	Novel RP-HPLC Method Development and Validation for Estimation of Pravastatin in Pure and Pharmaceutical Formulation.	A.Lakshmana Rao	Pharmaceutical Chemistry	Journal of Applied Pharmaceutical Sciences and Research.	2581-5520
14	Spectroscopical Method for Estimation of Atenolol and Hydrochlorothiazide in Pharmaceutical Dosage Form.	A.Sai Datri	Pharmaceutical Analysis	International Journal of Medical Laboratory Research	2546-4400
15	Spectroscopical Method for Estimation of Atenolol and Hydrochlorothiazide in Pharmaceutical Dosage Form.	A.Lakshmana Rao	Pharmaceutical Chemistry	International Journal of Medical Laboratory Research	2546-4400
16	Some Selected Phytoconstituents from *Rhus succedanea* as SARS CoV-2 Main Protease and Spike Protein (COVID-19) Inhibitors.	A.Lakshmana Rao	Pharmaceutical Chemistry	Iranain Journal of Pharmaceutical Sciences	1735-2444

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17	*In vivo* Antinociceptive effect of Methanolic Extract of *Ipomoea marginata* Desr. in Rodents as well as *In Silico* Molecular Docking of Some Phytoconstituents from the plant.	A.Lakshmana Rao	Pharmaceutical Chemistry	Indian Journal of Pharmaceutical Sciences.	0250-474X
18	Development and Evaluation of Controlled Release Formulations of Esomeprazole.	M.Sai Vishnu	Pharmaceutica	International Journal of Research in Ayush and Pharmaceutical Sciences.	2456-9909
19	Development and Evaluation of Controlled Release Formulations of Esomeprazole.	A.Lakshmana Rao	Pharmaceutical Chemistry	International Journal of Research in Ayush and Pharmaceutical Sciences.	2456-9909
20	Simultaneous Estimation of Ivacaftor and Tezacaftor in Rat Plasma by Liquid Chromatography Coupled with Tandem-Mass Spectrometry: Application to Pharmacokinetic Studies.	A.Lakshmana Rao	Pharmaceutical Chemistry	Thai Journal of Pharmaceutical Sciences.	1905-4637
21	Inhibitory effects of *Manosa alliacea* in Freund's adjuvant arthritis on inflammatory markers and its confirmation by *Insilico* strategy.	Sk.Aminabee	Pharmacology	Thai Journal of Pharmaceutical Sciences.	1905-4637
22	Inhibitory effects of *Manosa alliacea* in Freund's adjuvant arthritis on inflammatory markers and its confirmation by *Insilico* strategy.	A.Lakshmana Rao	Pharmaceutical Chemistry	Thai Journal of Pharmaceutical Sciences.	1905-4637

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23	*In-Silico* Strategies of Some Selected Phytoconstituents from *Melissaofficinalis* as SARS CoV-2 Main Protease and Spike Protein (COVID-19)	A.Lakshmana Rao	Pharmaceutical Chemistry	Molecular Simulation	1029-0435
24	Stability Indicating RP-HPLC Method Development and Validation for the Estimation of Ondansetron in Bulk and their Pharmaceutical Dosage Form.	A.Lakshmana Rao	Pharmaceutical Chemistry	International Journal of Research in Ayush and Pharmaceutical Sciences.	2456-9909
25	Simultaneous Estimation of Metformin and Teneligliptin in Pharmaceutical Formulation by using UV Spectroscopy.	A.Lakshmana Rao	Pharmaceutical Chemistry	International Journal of Research in Ayush and Pharmaceutical Sciences.	2456-9909
26	Formulation and Evaluation of Paracetamol Suspension by using Natural Suspending Agent Extracted from *Pedalium murex* Seeds.	M.Sai Vishnu	pharmaceutics	World Journal of Pharmacy and Pharmaceutical Sciences.	2278-4357
27	Formulation and Evaluation of Paracetamol Suspension by using Natural Suspending Agent Extracted from *Pedalium murex* Seeds.	A.Lakshmana Rao	Pharmaceutical Chemistry	World Journal of Pharmacy and Pharmaceutical Sciences.	2278-4357
28	Development and Validation of an LC-MS/MS Method for Determination of Atorvastatin in Human Plasma.	A.Lakshmana Rao	Pharmaceutical Chemistry	Asian Journal of Medicine and Health Sciences.	2456-8414

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29	Stability-Indicating Method Development and Validation for the Concurrent Determination of Darunavir, Cobicistat, Emtricitabine and Tenofovir Alafenamide by UPLC in Bulk and Tablet Dosage Forms.	A.Lakshmana Rao	Pharmaceutical Chemistry	Future Journal of Pharmaceutical Sciences	2314-7253
30	Bio-Analytical Method Development and Validation for Simultaneous Quantifi- cation of Glecaprevir and Pibrentasvir in Rat Plasma by Using RP-HPLC	T Prasanthi	Pharmaceutical Analysis	Journal of Drug and Alcohol Research	2090-8342
31	Estimation of Daclatasvir in Pharmaceutical Dosge Form by Ultra Performance Liquid Chromatography	A. Lakshmana Rao	Pharmaceutical Chemistry	International Journal of Pharmaceutical Sciences and Research	2320-5148
32	Stability-Indicating Method Development and Validation for the Concurrent Determination of Darunavir, Cobicistat, Emtricitabine and Tenofovir Alafenamide by UPLC in Bulk and Tablet Dosage Forms	A. Lakshmana Rao	Pharmaceutical Chemistry	Future Journal of Pharmaceutical Sciences	2314-7253

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33	Stability Indicating HPLC Method Development and Validation for the Simultaneous Estimation of Lamivudine and Dolutegravir in Bulk and Tablet Dosage Forms	A. Lakshmana Rao	Pharmaceutical Chemistry	Indian Drugs	0019-462X
34	Bio-Analytical Method Development and Validation for Simultaneous Quantifi cation of Glecaprevir and Pibrentasvir in Rat Plasma by Using RP-HPLC	Prasanthi T	Pharmaceutical Analysis	Journal of Drug and Alcohol Research	2090-8334

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Computational study for identifying promising therapeutic agents of hydroxychloroquine analogues against SARS-CoV-2

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ABSTRACT

Hydroxychloroquine (HCQ) and its derivatives have recently gained tremendous attention as a probable medicinal agent in the COVID-19 outbreak caused by SARS-CoV-2. An efficient agent to act directly in inhibiting the SARS-CoV-2 replication is yet to be achieved. Thus, the goal is to investigate the dynamic nature of HCQ derivatives against SARS-CoV-2 main protease and spike proteins. Molecular docking studies were also performed to understand their binding affinity *in silico* methods using the vital protein domains and enzymes involved in replicating and multiplying SARS-CoV-2, which were the main protease and spike protein. Molecular Dynamic simulations integrated with MM-PBSA calculations have identified *In silico* potential inhibitors ZINC05135012 and ZINC59378113 against the main protease with -185.171 ± 16.388, -130.759 ± 15.741 kJ/mol respectively, ZINC16638693 and ZINC59378113 against spike protein -141.425 ± 22.447, -129.149 ± 11.449 kJ/mol. Identified Hit molecules had demonstrated Drug Likeliness features, PASS values and ADMET predictions with no violations.

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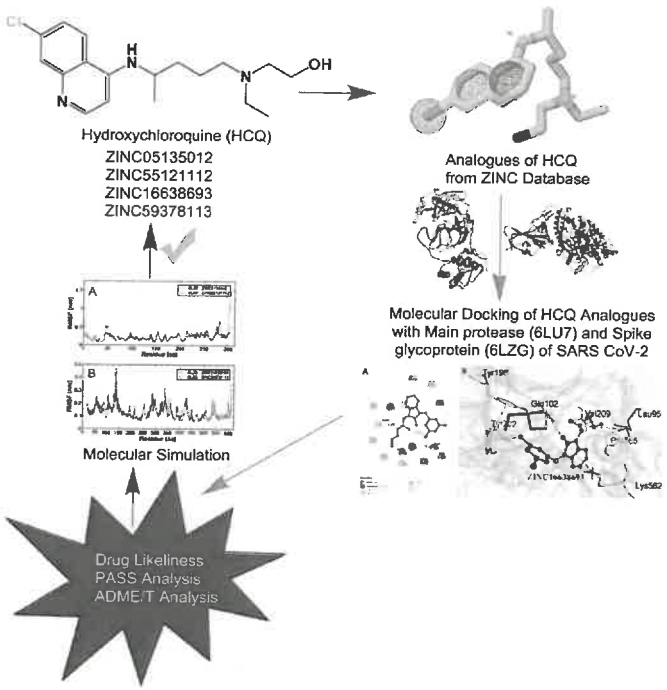
KEYWORDS
Hydroxychloroquine analogues; *in silico*; molecular dynamics; ADMET; PASS analysis



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Supplemental data for this article can be accessed online at https://doi.org/10.1080/07391102.2021.1965027

Current Pharmaceutical Analysis, 2021, *17*, 1060-1074

RESEARCH ARTICLE

BENTHAM SCIENCE

Development and Validation of a Method for Simultaneous Estimation of Sitagliptin and Ertugliflozin in Rat Plasma by LC-MS method

Pallepogu Venkateswara Rao[1,*], Atmakuri Lakshmana Rao[2] and Sahini Venkata Uma Maheswara Prasad[1]

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Abstract: ***Background*:** The development of sound bioanalytical LC-MS (liquid chromatography-mass spectroscopy) method(s) is of paramount importance during the process of drug discovery, development and culminating in a marketing approval. The use of oral antidiabetic agents has been increased significantly from the last decades and till now no bioanalytical method is available for quantitation of sitagliptin (SG) and ertugliflozin (EG) in biological matrix which can be applied to pharmacokinetic studies using LC-MS/MS.

***Objective*:** To develop a new, rapid and sensitive LC-MS/MS method for the simultaneous estimation of sitagliptin (SG) and ertugliflozin (EG) in rat plasma by Liquid-Liquid Extraction method (LLE) using deutereated sitagliptin (SGd6) and ertugliflozin (EGd6).

***Methods*:** Chromatographic separation was carried out on a reverse phase Waters, Xetrra C_{18} (150mm x 4.6mm, 2µm) column using a mixture of acetonitrile and OPA buffer (50:50v/v) at a flow rate of 1ml/min in isocratic mode. Quantification was achieved using an electrospray ion interface operating in positive mode, under Multiple Reaction Monitoring (MRM) conditions.

***Results*:** The method showed excellent linearity over the concentration range of 5.00- 75.00pg/mL for sitagliptin and 0.75- 11.35pg/mL ertugliflozin. The intra-batch and inter batch precision (%CV) was ≤ 4.3% and matrix effect (%CV) was 0.02% and 0.12% for sitagliptin at HQC and LQC, respectively. Matrix effect (%CV) was 0.08% and 0.33% for ertugliflozin at HQC and LQC, respectively.

***Conclusion*:** The simplicity of the method allows for application in laboratories, presents a valuable tool for pharmacokinetic studies. The particular assay has been proficiently put on pharmacokinetic study in rats subjects.

ARTICLE HISTORY

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Keywords: Development, validation, sitagliptin, ertugliflozin, rat plasma, LC-MS/MS.

1. INTRODUCTION

Type-2 Diabetes Mellitus (DM) is a chronic metabolic disorder in which prevalence has been increasing steadily all over the world. As a result of this trend, it is fast becoming an epidemic in some countries of the world with the number of people affected expected to double in the next decade due to an increase in the ageing population. Sitagliptin is an oral dipeptidyl peptidase-4 (DPP-4) inhibitor used in conjunction with diet and exercise to improve glycemic control in patients with type-2 diabetes mellitus [1]. The effect of this medication leads to glucose dependent increases in insulin and decreases in glucagon to improve control of blood sugar, Chemical name for Sitagliptin (Fig. **1**) is (3R)-3-amino-1[3(trifluoromethyl)-5H,6H,7H,8H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl]-4-(2,4,5-trifluorophenyl)butan-1-one. It has a molecular formula of $C_{16}H_{15}F_6N_5O$ and a molecular weight of 407.3 [2-4].

Ertugliflozin is in a class of medication called sodium-glucose co-trasporter 2 inhibitors belongs to glifolins class and used for the treatment of type2 diabetes. It lowers blood sugar level by causing the kidneys to get rid of more glucose in the urine. Chemically ertugliflozin (ERT) is (1S,2S,3S,4R,5S)5-(4-chlorp-3-(4-ethoxybenzyl)phenyl)-1-(hydroxymethyl)-6,8-dioxabicyclo octane-2,3,4-triol,with (2S)-5oxopyrrolidine-2-carboxylic acid (Fig. **2**). In the United States, it was approved by the FDA (Food & Drug Administration) for use as monotherapy and as affixed dose combination with either sitagliptin or metformin. It has a molecular formula of $C_{22}H_{25}ClO_7$ and a molecular weight of 436.89 [5-9].

Literature survey reveals that some chromatographic methods are available for estimation of sitagliptin alone and

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Original Article

Design, Synthesis, Hypoglycemic Activity and Molecular Docking Studies of 3-substituted-5-[(furan-2-yl)-methylene]-thiazolidine-2,4-dione Derivatives

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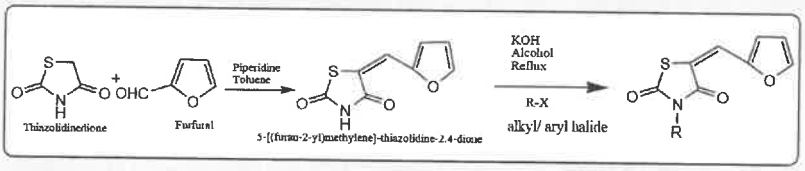
[1]Department of Pharmaceutical Chemistry, VV Institute of Pharmaceutical Sciences, Gudlavalleru, Andhra Pradesh, INDIA.
[2]Department of Chemistry, Krishna University, Machilipatnam, Andhra Pradesh, INDIA.

ABSTRACT

Background: From the wide range of previous literature studies indicated that thiazolidinedione's reacts with substituted benzaldehydes undergoes knoevenagel condensation gives respective arylidene derivatives. In our attempt all the titled compounds were designed and developed by replacement of substituted benzaldehydes with furan- 2-aldehyde, so that furan moiety was introduced in the molecule. **Materials and Methods:** 5-[(furan-2-yl)-methylene]-thiazolidine-2,4-dione was prepared via knoevenagel condensation by the reaction of thiazolidine-2,4-dione and furfural. Further it was coupled with various alkyl/ aryl halides in alcoholic potassium hydroxide to produce various derivatives 2a-2j. The titled compounds furthermore prepared by microwave assisted synthesis technique. Synthesized compounds were analysed by physical and spectral characterization methods. Developed furan bearing thiazolidine-2,4-diones were evaluated for *in-vivo* hypoglycemic property. Molecular docking analysis was carried out to observe the binding interaction of designed ligands at PPARγ target receptor protein. **Results and Conclusion:** Microwave irradiation technique produced high yield at less reaction time in comparison with traditional conventional method. *In-vivo* hypoglycemic activity evaluation revealed that, electron releasing groups (-OH and –OCH3) containing compounds 2d and 2g found to possess significant activity in acute study as well as in chronic study. Even the molecular docking studies at PPARγ receptor protein (PDB ID-2PRG), electron releasing groups containing compounds 2d and 2g exhibit significant binding affinity having high binding energy of -9.02 kcal/mol and -8.61 kcal/mol when compared with standard ligand rosiglitazone.



Key words: Thiazolidinedione derivatives, Synthesis, Hypoglycemic Activity, Molecular Docking, PDB ID-2PRG.

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INTRODUCTION

Diabetes mellitus (DM) is universally widespread chronic metabolic disorder during which elevated blood sugar levels take place over a prolonged period of time and symptoms comprises recurrent urination, increased hunger and thirsty. DM is allied with rigorous degenerative complications for instance nephropathy, cataract, neuropathy, accelerated atherosclerosis, retinopathy and stroke and increased the risk of myocardial infarction. Onset of these pathologies is a remarkable event throughout both

Original Article

Design, Synthesis, Hypoglycemic Activity and Molecular Docking Studies of 3-substituted-5-[(furan-2-yl)-methylene]-thiazolidine-2,4-dione Derivatives

Karumanchi Srikanth Kumar[1], Atmakuri Lakshmana Rao[1,*], Dachuru Rama Sekhara Reddy[2]

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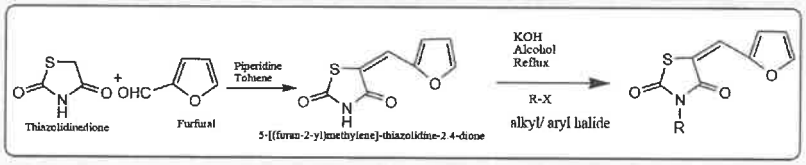

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Submission Date: 01-04-2020;
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INTRODUCTION

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Rapid quantitative estimation of metformin and ertugliflozin in rat plasma by liquid chromatography-tandam mass spectroscopy and its application to pharmacokinetic studies

P Venkateswarao Rao[a], A Lakshmana Rao[b], SVUM Prasad[c]

[a]Vikas college of Pharmacy, Vissannapeta and PhD Research Scholar, JNTUK Kakinada, AP, India, [b]V. V. Institute of Pharmaceutical Sciences, Gudlavalleru, AP, India, [c]School of Pharmacy, JNTUK Kakinada, AP, India

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Egyptian Pharmaceutical Journal 2021, 20:1–7

Background
The development of sound bioanalytical liquid chromatography-mass spectroscopy (LC-MS) method(s) is of paramount importance during the process of drug discovery and development, eventually culminating in marketing approval. The use of oral antidiabetic agents has been increased significantly from past decades, and till now, no bioanalytical method is available for quantitation of metformin (MET) and ertugliflozin (ERT) in the biological matrix that can be applied in bioequivalence studies using LC-MS/MS.

Objective
To study the use of highly responsive simple liquid–liquid extraction method development using deuterated MET and deuterated ERT, LC-MS/MS method for gradation of MET and ERT in the rat plasma.

Materials and methods
The chromatographic condition involves isocratic mode using Waters XBridge C_{18} 3.5 µ (150×4.6 mm) column. Mobile phase was 0.1% orthophosphoric acid and acetonitrile in the ratio of 80 : 20 v/v. Detection was carried out on a triple quadrapole MS employing electrospray ionization technique, operating multiple reactions, monitoring with the transitions of m/z 258.2→174.1, m/z 250.1→210.2, m/z 258.2→174.1, and m/z 260.3→210.2 for MET, ERT, deuterated MET, and deuterated ERT, respectively, in the positive ion mode.

Results and conclusion
The method has been validated, and the linearity was observed in the range of 10–150 ng/ml and 0.1–1.5 ng/ml for MET and ERT, respectively. For intraday and interday %RSD, the values were found to be within the acceptable limits. Recovery studies for MET and ERT obtained, mean recovery of 99.5 and 98.6%, respectively. A battery of stability studies like bench-top stability, autosampler stability, freeze-thaw stability, and long-term stability were performed. Highly responsive simple LC-tandem MS assay method was developed and witnessed for the gradation of MET and ERT in the rat plasma; the developed method was applied to pharmacokinetic studies.

Keywords:
ertugliflozin, liquid chromatography-mass spectroscopy, metformin, method validation, pharmacokinetic study

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Introduction

An oral antidiabetic drug used for the treatment of type 2 diabetes is metformin (MET), and chemically, it is 3-(diaminomethylidene)-1, 1-dimethylaniline (Fig. 1). MET is an oral antihyperglycemic agent of the biguanide class and used for the treatment of type 2 diabetes. MET is the first drug of choice for the treatment of type 2 diabetes. So MET is considered as an antihyperglycemic agent because it lowers blood glucose concentration in type 2 diabetes without causing hypoglycemia. Control of high blood sugar levels helps to prevent kidney damage, nerve problems, blindness, loss of limbs, and sexual problems. MET helps restore body's proper response to the insulin as well as helps in the natural production of insulin. It also decreases the amount of sugar level made by the liver and that absorbed by the stomach and intestines [1–6].

Ertugliflozin (ERT) is in a class of medication called sodium-glucose cotransporter 2 inhibitors, which belongs to gliflozin class and is used for the treatment of type 2 diabetes. It lowers blood sugar level by causing the kidneys to get rid of more glucose in the urine. Chemically, ERT is (1S,2S,3S,4R,5S)5-(4-chlorp-3-(4-ethoxybenzyl)phenyl)-1-(hydroxymethyl)-6,8-dioxabicyclo octane-2,3,4-triol, with (2S)-5oxopyrrolidine-2-carboxylic acid (Fig. 2). In the United states, it was approved by the FDA for use as monotherapy and as affixed dose combination with either sitagliptin or MET [7–10].

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Research Article

VALIDATION OF A DEVELOPED ANALYTICAL METHOD FOR DETERMINATION OF NATEGLINIDE AND METFORMIN HCL IN PURE AND PHARMACEUTICAL DOSAGE FORM BY REVERSED-PHASE HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY AND ITS DEGRADATION STUDIES

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ABSTRACT

Objective: The objective of the study was to develop a versatile analytical method and validate according to International Council for Harmonization guidelines for simultaneous estimation of nateglinide and metformin HCl by reversed-phase high-performance liquid chromatography (RP-HPLC) in active pharmaceutical ingredient and in tablet dosage form.

Methods: Analytes, metformin and nateglinide, are separated and eluted from stationary phase luna phenyl hexyl column (150 mm ×4.6 mm, 3.5 µm) (micrometer) using polar mobile phase composed of acetonitrile:1% orthophosphoric acid 30:70 v/v, with flow rate of 1 ml/min for 8 min at ambient column temperature, at 221 nm (nanometer) detection. Acid, base, peroxide, thermal, and photolytic-induced degradation studies were performed on nateglinide and metformin.

Results: Through isocratic flow, both metformin and nateglinide are detected at retention times of 2.79 min and 5.13 min, respectively, at 221 nm. The linearity and range of analytical method for nateglinide and metformin were 0.61–9.15 µg/ml and 7.5–75.15 µg/ml, respectively. The R^2 value for nateglinide was 0.9998 and for metformin HCl was 0.9991. The limit of detection and limit of quantification for nateglinide were 0.21 µg/ml and 0.63 µg/ml and for metformin were 4.8 µg/ml and 14.6 µg/ml, respectively. The % relative standard deviation for method precision was found to be 0.22% and 0.64% for both nateglinide and metformin, respectively. The mean %recovery for nateglinide and metformin was 99.88% and 99.21%, respectively. The %thermal degradation was identified as 17.7% and 17.5% for nateglinide and metformin, respectively.

Conclusion: The developed chromatographic (RP-HPLC) method was selective, specific, economic, precise, and accurate. Hence, it can be one of the preferred analytical methods of choice for the estimation of nateglinide and metformin by RP-HPLC in pure and in tablet dosage form.

Key words: Nateglinide, Metformin, Reversed-phase high-performance liquid chromatography, Isocratic, Acetonitrile.

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INTRODUCTION

Nateglinide is chemically 3-phenyl-2-[(4-propan-2-yl cyclohexane carbonyl) amino] propanoic acid (Fig. 1) with molecular formula $C_{19}H_{27}NO_3$. It acts by blocking adenosine triphosphate sensitive potassium channels of beta cells of pancreas, causes membrane depolarization results in calcium influx and their by stimulation of insulin secretion. Metformin HCl is chemically N, N-Dimethyl imidodicarbonimidic diamide hydrochloride (Fig. 2) with molecular formula $C_4H_{11}N_5$.HCl. The main mechanism of metformin HCl was lowering glucose intestinal absorption, inhibition of hepatic glucose production, and improving glucose uptake and utilization [1-6].

It was found that very few articles are available in detailed literature survey on simultaneous estimation of nateglinide and metformin HCl by reversed-phase high-performance liquid chromatography (RP-HPLC) in pure and dosage form [7-9]. The resting literature was found on analytical and bioanalytical methods by HPLC, LC–MS/MS, RP-LC, high-performance thin-layer chromatographic, and ultraviolet (UV) spectrophotometric estimations, in combination with glinides (nateglinide, repaglinide, and mitiglinide) and metformin HCl [10-21].

The comprehensive literature survey disclosed diverse analytical techniques of estimating nateglinide and metformin HCl in single and in combination with other drugs. The present study was taken up to develop a sensitive, accurate, precise, and simple method of analysis for the estimation of both drugs in combined dosage forms.

METHODS

Chemicals and reagents

The active pharmaceutical ingredients (APIs), nateglinide and metformin hydrochloride, were supplied as a gift sample by Care Labs, L.B Nagar, Hyderabad, and marketed formulation was purchased from the local market. HPLC grade orthophosphoric acid, acetonitrile, and water were of Merck grade. Waters autosampler RP-HPLC, e2695 pump, and 2998 photodiode array (PDA) detector with Empower2 software were employed in this method.

Selection and preparation of mobile phase and diluent

In RP-HPLC, pure API mixture containing nateglinide and metformin HCl at lower concentration levels were prepared, injected, and run with different solvent systems. Different combination of solvents using acetonitrile, triethylamine, and orthophosphoric acid at different compositions, flow rates, and ratios were tried to optimize the mobile phase. Finally from the trials, mobile phase and diluent (acetonitrile and 0.1% orthophosphoric acid in a ratio of 30:70 v/v) are selected since they were fulfilling the requirements and the results obtained were within the acceptable limits.

Preparation of standard stock solution

Powder analytes equivalent to 6 mg and 50 mg of nateglinide and metformin HCl, respectively, were accurately weighed and transferred

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RESEARCH ARTICLE

Antidiabetic Activity of Methanolic Extract of *Searsia mysorensis* in Alloxan Induced Diabetic Rats

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ABSTRACT

This dreadful disease is found in all parts of the world and is becoming a serious threat to the mankind. There are a lot of chemical agents available to control and to treat diabetic patients but total recovery from diabetes has not been reported up to this date. Alternative to these synthetic agents' plants provide a potential source of hypoglycemic drugs and are used widely in several traditional systems of medicine to prevent diabetes. The aim of the present study was to evaluate the antidiabetic activity of methanolic leaf extract of *Rhus mysorensis* in alloxan-induced diabetic rats.

Keywords: Antidiabetic, Methanolic, Searsia mysorensis

INTRODUCTION

Traditional medicine is looked on as an alternative or supplement to modern medicine and has made significant contributions to the healthcare of the world over the past decades. Various diseases such as diarrhea, skin problems, headache, fever, cough, wounds, hypertension, diabetes, and rheumatism are treated with herbal medicine. Traditional medicines continue to be practiced by the community to treat disease and maintain health especially in remote areas where modern facilities are not readily available. Most of the medicinal plant species are collected from the wild, a few are being cultivated.[1]

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DIABETES MELLITUS

Diabetes mellitus commonly known as diabetes is a group of metabolic disorder characterized by high glucose blood level over a prolonged period of time.[2] Diabetes is due to either pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.[3]

Types of diabetes mellitus

WHO classified diabetes mellitus into three types based on the etiology.[4]

- Type 1 diabetes (Insulin Dependent Diabetes Mellitus [IDDM])
- Type 2 diabetes (Non-IDDM)
- Gestational diabetes.

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ESTIMATION OF DACLATASVIR IN PHARMACEUTICAL DOSAGE FORM BY ULTRA PERFORMANCE LIQUID CHROMATOGRAPHY

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Keywords:

UPLC, Daclatasvir, Orthophosphoric acid, Acetonitrile

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ABSTRACT: Daclatasvir is an antiviral drug used in combination with other drugs includes sofosbuvir, ribavirin, and interferon, depending on the virus type to treat cirrhosis caused by hepatitis C (HCV). Several methods have been found for quantification, but those are not cost-effective, and they are time-consuming. The present study developed a simple, precise, accurate and cost-effective UPLC method to determine daclatasvir quantity in tablet dosage forms. A simple and selective UPLC method is described for the determination of Daclatasvir Chromatographic separation was achieved on a Acquity BEH C18 (50 × 3.0mm. 1.7 µm) using a mobile phase consisting 0.1% of Orthophosphoric acid: Acetonitrile in a ratio of 60:40 v/v with detection of 248 nm. Linearity was observed in the range 50-150 µg/ml for Daclatasvir (r^2 = 1.000). The amount of drugs estimated by the proposed method was in good agreement with the label claim. The proposed method was validated as per ICH guidelines and applied for the determination of the cited drug in the dosage form.

INTRODUCTION: Daclatasvir is chemically dimethyl N, N'-([1,1'-biphenyl]-4, 4'-diylbis{1H-imidazole-5,2-diyl-[(2S)-pyrrolidine-2,1-diyl][(2S)-3- methyl- 1- oxobutane-1, 2-diyl]}) dicarbamate. Daclatasvir has molecular weight: 738.89 g/mol and molecular formula: $C_{40}H_{50}N_8O_6$. It is an antiviral drug used in combination with other medicaments to treat hepatitis C (HCV). The other medicines used in combination include interferon, sofosbuvir, and ribavirin, depending on the virus type 1. The dose of daclatasvir present in the formulation was determined by using the Ultra Performance Liquid Chromatography method. UPLC has greater sensitivity, resolution, and speed of analysis.

QUICK RESPONSE CODE

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UPLC operates at high pressure than HPLC, and fine particles, *i.e.*, less than 2.5 µm are used, and mobile phases at high linear velocities decrease the length of the column, reduces solvent consumption, and save time [2].

The UPLC is based on the use of a stationary phase consisting of particles less than 2.5 µm whereas the HPLC column is typically filled with 3-5 µm particles. The principle of this evolution is governed by the Van Deemeter equation, which is an empirical formula that describes the relationship between the linear velocity of flow rate and plate height [3, 4].

$$H = A + B / v + Cv$$

Where; A, B and C are constants, v is the linear velocity, the carrier gas flow rate.

*The A term is independent of velocity and represents "eddy" mixing. It is the smallest when the packed column particles are small and uniform.

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RESEARCH ARTICLE

Development of Metoprolol Tartrate Sustained Release Formulations by using Modified Starches

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ABSTRACT

This study is aimed to design oral sustained-release formulations for the anti-hypertension drug Metoprolol tartrate. This drug exhibits required physicochemical and pharmacokinetic parameters to formulate sustained-release formulations. The literature survey reveals that Sustained Release formulations for some drugs were prepared by employing Modified Starch known as Calcium Starch. Natural Starches such as potato starch, rice starch, and corn starches can be chemically modified using cross-linking agents such as calcium chloride and it may be used as release retardants. The functional characteristics of starch may vary from source to source. Hence, there is a scope to evaluate the effect of starch on release characteristics of the drug. Further, the drug release is expected to be altered by the proportion of release retardant and hence there is a need to optimize the composition by screening the composition. Hence, there is scope for comparative evaluation of modified starches prepared using different naturally occurring starches and their effect on release characteristics of metoprolol tartrate for sustained release formulations.

Keyword: Metoprolol, Starch, Tartrate

INTRODUCTION

Starch is a natural, cheap, available, renewable, and biodegradable polymer produced by many plants as a source of stored energy. It is the second most abundant biomass material in nature. It is found in plant leaves, stems, roots, bulbs, nuts, stalks, crop seeds, and staple crops such as rice, corn, wheat, cassava, and potato. From serving as food for man, starch has been found to be effective in drying up skin lesions (dermatitis), especially where there are watery exudates consequently, starch is a major component of dusting powders, pastes, and ointments meant to provide protective and healing effect on skins. Starch mucilage has also performed emollient and major base in enemas. Because of its ability to form complex with iodine, starch has been used in treating iodine poisoning. Acute diarrhea has also been effectively prevented or treated with starch-based solutions due to the excellent ability of starch to take up water. In pharmacy, starch appears indispensable; it is used as excipients in several medicines. Its traditional role as a disintegrate or diluents is giving way to the more modern role as drug carrier; the therapeutic effect of the starch-adsorbed or starch-encapsulated or starch-conjugated drug largely depends on the type of starch.

Basic structural design of starch

Starch, which is the major dietary source of carbohydrates, is the most abundant storage polysaccharide in plants and occurs as granules in the chloroplast of green leaves and the amyloplast

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Review Article

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A Review on Inductively Coupled Plasma: Mass Spectrometry with Laser Ablation

[1]Sai Datri A, [2]Nataraj KS, [3]Lakshmana Rao A

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Abstract

Inductively coupled plasma mass spectrometry (ICP-MS) is a kind of mass spectroscopy which is used in many diverse research fields such as earth, environmental, life and forensic sciences and in food, material, chemical, semiconductor and nuclear industries. In this sort of MS, Laser ablation (LA) ICP-MS is widely used to determine elements directly in virtually all types of solid samples with minimal sample preparation. UV lasers are widely used with ICP-MS because of their highly controllable spatial resolution (spot size) and relatively low cost. This technique is used to determine low-concentrations and even ultra-low-concentrations of elements. Atomic elements are lead through a plasma source where they become ionized. The high ion density and the high temperature in plasma provide an ideal atomizer and element ionizer for all types of samples and matrices introduced by a variety of specialized devices. Then, these ions are sorted on account of their mass. ICP-MS holds a distinctive position by virtue of its speed, sensitivity, dynamic range and elemental coverage. It can be considered as a viable alternative to ICP-Optical Emission Spectroscopy (OES) (also known as Atomic Emission Spectroscopy or AES) for fast measurement of higher concentration elements. At the same time, ICP-MS in many cases exceeds the detection capability of Graphite Furnace Atomic Absorption Spectroscopy (GFAAS) for the determination of trace and ultra-trace elements (ng/L or ppt concentrations). One of the fastest growing areas of ICP-MS is in speciation measurement: the combination of chromatographic techniques with ICP-MS as a detector to determine the chemical form of elements in the sample. This review provides an overview of recent developments and abilities of inductively coupled plasma mass spectrometry (ICPMS) coupled with different separation techniques for applications in the field of analysis and also highlighted numerous technical improvements, over the past few years which helped to promote the evolution of ICP-MS to one of the most versatile tools for elemental quantification as Laser ablation (LA) ICP-MS. In particular, the benefits and possibilities of using state-of-the-art hyphenated ICP-MS approaches for quantitative analysis applications.

Keywords: Inductively couple plasma mass spectrometry; ICP-MS; Laser ablation; Hyphenated techniques; Quantification and Trace elements.

Introduction

Inductively coupled plasma mass spectrometry[1] (ICP-MS) is a type of mass spectroscopy which is used in many diverse research fields. This technique is used to determine low-concentrations and even ultra-low-concentrations of elements. While many sampling methods have been investigated for use with ICP-MS, some have become outdated, or remain of academic interest, such as spark ablation and slurry nebulization for solids analysis, and electro thermal vaporization (ETV) as a sample introduction device.

Review Article

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A Review on Inductively Coupled Plasma: Mass Spectrometry with Laser Ablation

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Abstract

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Keywords: Inductively couple plasma mass spectrometry; ICP-MS; Laser ablation; Hyphenated techniques; Quantification and Trace elements.

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RESEARCH ARTICLE

Novel RP-HPLC Method Development and Validation for Estimation of Pravastatin in Pure and Pharmaceutical Formulation

Prasanthi T [1*], Lakshmana Rao A[2], Reshma P[3], Susanthi P[3], Merwin P[3], Ajay P[3]

Abstract

Introduction: A simple, rapid, precise, accurate, sensitive and stability indicating RP-HPLC method for the determination of Pravastatin in pure and tablet dosage form.

Materials & Methods: HPLC Method was developed using Zorbax ODS (250×4.6 mm ×5 µ) with the mobile phase of 0.1% formic acid pH adjusted to 3 and methanol in the ratio 50:50 v/v. Pravastatin peak was monitored at 238 nm, and the retention time was 4.44 minutes.

Results and Discussion: ICH guidelines were followed to validate the proposed method regarding specificity, precision, linearity, accuracy, system suitability, and robustness. The method was found to be linear in the range of 10–50 µg/mL, and also the regression equation was found to be y=124936 x+19884 R^2=0.997. For intra- and inter-day precision, the %RSD for Pravastatin was 1.05 and 0.917%. Percentage mean recovery was found to be 98.36%. LOD and LOQ values were 0.231 and 0.701 µg/mL, respectively. Pravastatin stability was inspected under various forced degradation conditions, and it was found to be easily degraded in acidic and basic conditions.

Conclusion: The developed method was found to be having a suitable application for routine quality control analysis of Pravastain in pharmaceutical formulations.

Keywords: Degradation, Pravastatin, RP-HPLC. Validation.

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Introduction

Pravastatin is chemically known as (3R,5R)-7-[(1S,2S,6S,8S,8aR)-6-hydroxy-2-methyl-8-{[(2S)-2-methylbutanoyl]oxy}-1,2,6,7,8,8a-hexahydronaphthalen-1-yl]-3,5-dihydroxyheptanoic acid.[1] Pravastatin (Figure 1) is a specific inhibitor of the hepatic HMG-CoA reductase in humans. The inhibition of this enzyme produces a reduction in cholesterol biosynthesis as HMG-CoA reductase activity is an early-limiting step in cholesterol biosynthesis.[2] Pravastatin is also used to lower the risk of stroke, heart attack, and other heart complications.[3]

Literature survey reveals that very few HPLC[4-8] methods were reported to estimate Pravastatin in pharmaceutical dosage forms. In the present work an attempt has been made to develop a novel, rapid and economic RP-HPLC method for estimation of Pravastatin in pure and tablet dosage form.

Materials and Methods

Instrument

Agilent 1260 infinity binary pump HPLC equipped with PDA detector and EZ Chrome open lab software was used for chromatographic studies. The column used was Zorbax ODS with dimensions 250 mm×4.6 mm ×5 µ.

Chemicals

Pravastatin pure drug was purchased from Yarrow Chemicals, Mumbai. HPLC grade methanol, formic acid, and all other chemicals were purchased from Merck Limited, Mumbai. Triple distilled water was used throughout the study. Pravastatin tablets were procured from local pharmacy.

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Conflict of interest: None

Preparation of Standard Stock Solution

A standard stock solution was prepared by dissolving 10 mg of Pravastatin in 10 mL mobile phase, then sonicated for about 10 minutes to get the primary standard stock solution containing 1000 µg/mL of Pravastatin. Working standard solution was prepared by further dilution with mobile phase.

RESEARCH ARTICLE

Novel RP-HPLC Method Development and Validation for Estimation of Pravastatin in Pure and Pharmaceutical Formulation

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Introduction: A simple, rapid, precise, accurate, sensitive and stability indicating RP-HPLC method for the determination of Pravastatin in pure and tablet dosage form.

Materials & Methods: HPLC Method was developed using Zorbax ODS (250×4.6 mm ×5 µ) with the mobile phase of 0.1% formic acid pH adjusted to 3 and methanol in the ratio 50:50 v/v. Pravastatin peak was monitored at 238 nm, and the retention time was 4.44 minutes.

Results and Discussion: ICH guidelines were followed to validate the proposed method regarding specificity, precision, linearity, accuracy, system suitability, and robustness. The method was found to be linear in the range of 10–50 µg/mL, and also the regression equation was found to be y=124936 x+19884 R^2=0.997. For intra- and inter-day precision, the %RSD for Pravastatin was 1.05 and 0.917%. Percentage mean recovery was found to be 98.36%. LOD and LOQ values were 0.231 and 0.701 µg/mL, respectively. Pravastatin stability was inspected under various forced degradation conditions, and it was found to be easily degraded in acidic and basic conditions.

Conclusion: The developed method was found to be having a suitable application for routine quality control analysis of Pravastain in pharmaceutical formulations.

Keywords: Degradation, Pravastatin, RP-HPLC. Validation.

Journal of Applied Pharmaceutical Sciences and Research, (2022); DOI: 10.31069/japsr.v4i3.3

Introduction

Pravastatin is chemically known as (3R,5R)-7-[(1S,2S,6S,8S,8aR)-6-hydroxy-2-methyl-8-{[(2S)-2-methylbutanoyl]oxy}-1,2,6,7,8,8a-hexahydronaphthalen-1-yl]-3,5-dihydroxyheptanoic acid.[1] Pravastatin (Figure 1) is a specific inhibitor of the hepatic HMG-CoA reductase in humans. The inhibition of this enzyme produces a reduction in cholesterol biosynthesis as HMG-CoA reductase activity is an early-limiting step in cholesterol biosynthesis.[2] Pravastatin is also used to lower the risk of stroke, heart attack, and other heart complications.[3]

Literature survey reveals that very few HPLC[4-8] methods were reported to estimate Pravastatin in pharmaceutical dosage forms. In the present work an attempt has been made to develop a novel, rapid and economic RP-HPLC method for estimation of Pravastatin in pure and tablet dosage form.

Materials and Methods

Instrument

Agilent 1260 infinity binary pump HPLC equipped with PDA detector and EZ Chrome open lab software was used for chromatographic studies. The column used was Zorbax ODS with dimensions 250 mm×4.6 mm ×5 µ.

Chemicals

Pravastatin pure drug was purchased from Yarrow Chemicals, Mumbai. HPLC grade methanol, formic acid, and all other chemicals were purchased from Merck Limited, Mumbai. Triple distilled water was used throughout the study. Pravastatin tablets were procured from local pharmacy.

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Source of support: Nil

Conflict of interest: None

Preparation of Standard Stock Solution

A standard stock solution was prepared by dissolving 10 mg of Pravastatin in 10 mL mobile phase, then sonicated for about 10 minutes to get the primary standard stock solution containing 1000 µg/mL of Pravastatin. Working standard solution was prepared by further dilution with mobile phase.

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IJMLR International Journal of Medical Laboratory Research

RESEARCH ARTICLE

SPECTROSCOPICAL METHOD FOR ESTIMATION OF ATENOLOL AND HYDROCHLOROTHIAZIDE IN PHARMACEUTICAL DOSAGE FORM

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Received: 12 Aug, 2021/Revision: 13 Sep, 2021 /Accepted: 11 Nov, 2021

ABSTRACT: Introduction: A sensitive and validated spectroscopic estimation of Atenolol and Hydrochlorothiazide in pharmaceutical dosage form, without prior separation, by three different techniques (Simultaneous Equation, Dual Wavelength Method, and Derivative Spectroscopic Method) has been developed. Method: The works were carried out on Shimadzu electron UV1800 double beam UV-Visible spectrophotometer. The absorption spectra of reference and test solutions were carried out in 1 cm matched quartz cell over the range of 200 - 400 nm. The linearity ranges for Atenolol and Hydrochlorothiazide were 2-10 µg/ml and 1-5 µg/ml. Conclusion: The results of the analysis have been validated statistically and by recovery studies. The proposed procedures are rapid, simple, require no preliminary separation steps, and can be used for routine analysis of both drugs in quality control laboratories.

KEYWORD: Atenolol, Hydrochlorothiazide, UV spectroscopy, and Validation.

INTRODUCTION:

Chemically, Atenolol (Figure 1) is *(RS)-4-2(2-hydroxy-3-isopropyl amino propoxy) phenylacetamide*. It is a selective beta-1 adrenergic receptor antagonist. It is used in the treatment of cardiovascular diseases such as angina, hypertension, cardiac arrhythmias, and myocardial infarctions. Atenolol competitively blocks beta-adrenergic receptors in the heart and juxtaglomerular apparatus. They lead to decreased heart rate decreasing the workload of the heart. They do not produce coronary vasodilatation but lead to a shift and redistribution of the coronary circulation to the ischemic areas.

It decreases the release of renin from the kidney, thus lowering blood pressure. [1] Chemically, Hydrochlorothiazide (Figure 1) is *6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfanamide 1,1-dioxide*. It is a diuretic used for the treatment of edema associated with heart (congestive heart failure), liver (hepatic cirrhosis), renal (nephritic syndrome, chronic renal failure, and glomerulonephritis) diseases. Hydrochlorothiazide acts on the kidneys to reduce sodium (Na) reabsorption in the distal convulated tubule. [2]

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IJMLR *International Journal of Medical Laboratory Research*

RESEARCH ARTICLE

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www.ijps.ir

Original Article

Some Selected Phytoconstituents from *Rhus succedanea* as SARS CoV-2 Main Protease and Spike protein (COVID-19) Inhibitors

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Abstract

Rhus succedanea (Anacardiaceae) was used to treat multiple human afflictions. Literary works demonstrate that it has many biological activities. Today's research aims to recognize Rhus succedanea Phyto-derived anti-viral compounds against the main protease and spike protein of the viral agent of COVID-19 (SARS-CoV-2) gain insight into the molecular interactions. In the current study, ten molecules taken from *R. succedanea* are analyzed through docking, derived from the PubChem database. Docking experiments with Autodock vina and PyRx tools were conducted. AdmetSAR and DruLito servers were eventually used for drug-like prediction. Our research shows that the phytoconstituents from *R. succedanea*, namely, Amentoflavone, Rhoifolin, and Agathisflavone acts against SARS CoV-2 main protease with the binding affinity of -9.3, -8.6 and -8.4 Kcal/mol; Hinokiflavone Robustaflavone and Amentoflavone acts against the SARS-CoV-2 receptor-binding domain of spike protein with a binding affinity of -10.5, -10.4 and -10.1 Kcal/mol respectively. These phyto-compounds can use contemporary strategies to develop effective medicines from natural origins. The substances identified potential anti-viral as likely. However, *In-vitro* studies are even more necessary to assess their effectiveness versus SARS CoV-2.

Keywords: ADMET, In-silico, Lipinski's Rule, PyRx, Rhus succedanea.

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1. Introduction

WHO has currently stated a typical emergency and pandemic for the novel coronavirus (SARS CoV-2) that has proactively propagated worldwide. The virus SARS-CoV-2 can easily trigger signs and symptoms such as fever, coughing, pneumonia, nausea, as well as

Research Paper

In vivo Antinociceptive Effect of Methanolic Extract of *Ipomoea marginata* Desr. in Rodents as well as *In silico* Molecular Docking of Some Phytoconstituents from the Plant

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Department of Chemistry, Gudlavalleru Engineering College, Gudlavalleru 521356, [1]Pharmacognosy Research Division, K L College of Pharmacy, Koneru Lakshmaiah Education Foundation, Vaddeswaram, Guntur, [2]Department of Pharmaceutical Analysis, Vallabhaneni Venkatadri Institute of Pharmaceutical Sciences, Gudlavalleru 521356, Andhra Pradesh, India

This research was performed to analyze the antinociceptive task of methanolic extract of *Ipomoea marginata* in addition to *in silico* evaluation of the antinociceptive task of the separated constituents from *Ipomoea marginata* versus cyclooxygenase 2 enzyme together with absorption, distribution, metabolism, excretion/toxicity analysis of separated substances. *In vivo* antinociceptive task of methanolic extract of *Ipomoea marginata* was examined by acetic acid-induced agonizing, tail immersion and the hot plate on rodents. *In silico* activity of the isolated substances, absorption, distribution, metabolism, excretion/toxicity assessment was carried out by Autodock 4.0 and data warrior software applications. The results revealed that methanolic extract of *Ipomoea marginata* has the greatest possible dose-dependent antinociceptive task at all doses. Amongst the substances, Ipalbidine showed the very best docking score of -8.26, which was virtually better than standard diclofenac, i.e., -7.03, guaranteeing good binding compatibility among the ligand and the receptor than the standard and absorption, distribution, metabolism, excretion/toxicity evaluation using data warrior assures the compound has not breached Lipinski's guideline of five suggesting its safety consumption. To conclude, *Ipomoea marginata* can be a potent resource of antinociceptive activity and also additional simulation studies are needed to develop the performance of Ipalbidine.

Key words: *Ipomoea marginata*, leucorrhoea, depression, analgesic

Pain is a beneficial tool for the body's immune system to safeguard the location harmed by various stimulations. To care for the pain, vast arrays of antinociceptive like nonsteroidal anti-inflammatory drugs (NSAIDs), steroidal medicines in addition to opioid anaesthetics are utilized, which have a different harmful effect such as hepatic damage, cardio troubles, kidney failure, erectile dysfunction, manic depression, high blood pressure, aches as well as dizziness, look of inactive diabetes mellitus, skin degeneration, reduced bone density, intestinal system, abscess, reliance, constipation and also respiratory problems. So, it is crucial to the globe to make sure a resource of cost-abusing herbal-based antinociceptive medicines with more potent and less negative results may be acquired with the medicinal plant[1-4].

Molecular docking is an essential strategy of making plans and designing new drugs, where it is expected that a tiny molecule will certainly show affinity and bind experimentally to the binding site of the target receptor. Therefore, a practical docking approach must adequately forecast the native ligand model to the receptor-binding site and the linked physico-chemical molecular communications[5-8].

Ipomoea marginata (*I. marginata*) Verdc. (Family Convolvulaceae) is a perennial twiner with ovate-cordate acute leaves having reddish patches; light pink (having a dark eye), funnel-shaped flowers in pedunculate subumbellate cymes and ovoid, glabrous

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International Journal of Research in AYUSH and Pharmaceutical Sciences

Research Article

Development and Evaluation of Controlled Release Formulations of Esomeprazole

K. Deepika, M. Sai Vishnu*, A. Lakshmana Rao

Department of Pharmaceutics, V. V. Institute of Pharmaceutical Sciences, Gudlavalleru, A.P.

ARTICLE INFO

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Keywords: Esomeprazole, Eudragit-S100, Eudragit-L100, Eudragit-RSPO, Eudragit-RS100, Eudragit-RL100, Eudragit RLPO.

ABSTRACT

The present work was aimed to development of controlled release formulations of Esomeprazole to improve bioavailability. Esomeprazole is the proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H+/K+-ATPase in the gastric parietal cell. By acting specifically on the proton pump, Esomeprazole blocks the final step in acid production, thus reducing gastric acidity. Construction of calibration curve of Esomeprazole and to investigate the drug and polymer interaction studies by FTIR and DSC. To prepare the different controlled release formulations of Esomeprazole tablets with different polymers like Polymethacrylates such as Eudragit-S100, Eudragit-L100, Eudragit-RSPO, Eudragit-RS100, Eudragit-RL100 and Eudragit RLPO by Direct Compression method. Evaluation of Esomeprazole pre compression parameters such as Bulk density, Tapped density, Hausner's ratio, Carr's index, Angle of repose. Evaluation of post-compression parameters of Esomeprazole controlled release tablets such as Weight variation, Hardness, Friability test, Thickness, Drug Content and *In-vitro* dissolution studies. Evaluation of *in-vitro* dissolution uniqueness of all the formulations of Esomeprazole by using USP dissolution apparatus type-II (paddle). To study the mechanism of drug dissolution by applying kinetic parameters. To perform the stability studies of optimized formulations of Esomeprazole as per ICH guidelines.

INTRODUCTION

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to acquire quick and entire systemic drug absorption. Such immediate release products result in comparatively rapid drug absorption and onset of associated pharmacodynamic effects. Although, after absorption of the drug from the dosage form is whole, plasma drug concentrations refuse according to the drugs PK profile. Ultimately plasma drug concentrations reduce below the minimum effective plasma concentration (MEC), ensuing in loss of therapeutic activity. Before this point is reached, another dose is frequently given if a sustained therapeutic effect is required. A substitute to administer an additional dose is to use a dosage form that will afford sustained drug release, and hence maintain plasma drug concentrations, ahead of what is typically seen using immediate release dosage forms.

MATERIALS AND METHODS

Esomeprazole is highly effective inhibitor of gastric acid secretion used in the therapy of stomach ulcers and zollinger-ellison syndrome. The drug inhibits the H(+)-K(+)-ATPase (H(+)-K(+)- exchanging ATPase) in the proton pump of gastric parietal cells.

Structure:

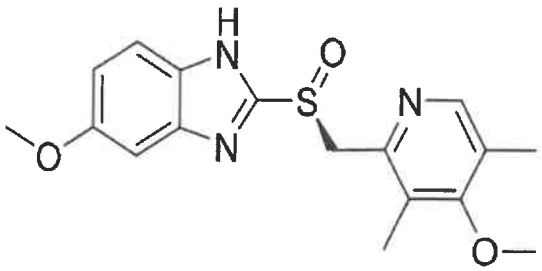

Figure No: 1 Structure of Esomeprazole

Chemical Formula: $C_{17}H_{19}N_3O_3S$

Molecular weight: Average: 345.416, Monoisotopic: 345.114712179 g/mol.

ISSN: 2456-9909 (Online)

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Research Article

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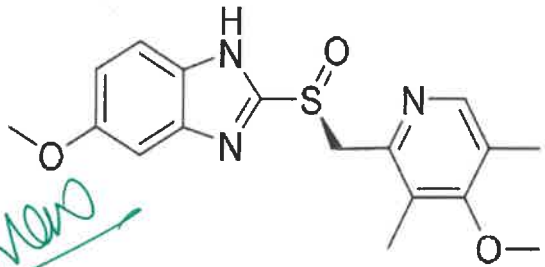

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Molecular weight: Average: 345.416, Monoisotopic: 345.114712179 g/mol.

Original Article

Thai Journal of Pharmaceutical Sciences

Simultaneous estimation of ivacaftor and tezacaftor in rat plasma by Liquid chromatography coupled with tandem-mass-spectrometry: Application to pharmacokinetic studies

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ABSTRACT

Background: Ivacaftor and Tezacaftor belong to the CFTR potentiator class, in combination approved to manage cystic fibrosis. **Objective:** To establish a sensitive LC-MS/MS approach for the synchronized analysis of Ivacaftor and Tezacaftor and its appliance to rat pharmacokinetic investigation. **Methodology:** Method is developed with protein precipitation by acetonitrile and Ivacaftor-d4, Tezacaftor-d4 are used as internal standards. Separation is done on an Eclipse plus C18 analysis column (100 mm × 4.6 mm 1.8 μm) with a mobile phase consisting of 0.1% trifluoroacetic acid: acetonitrile (ratio 60:40, v/v, and pH 2.5) and flow stream of 1.0 mL/min at ambient temperature. **Results:** The approach developed showed fine calibration curve in the quantity range of 1.5-22.53 ng/mL (r2 – 0.99974) for ivacaftor and 1-15.02 ng/mL (r2 – 0.99988) for tezacaftor and the accuracy and precision meets F.D.A guidelines. **Conclusion:** The newly designed and validated approach was simple, fast and applied effectively for rat pharmacokinetic investigation.

Keywords: Ivacaftor, Tezacaftor, LC-MS/MS, Method Validation, Pharmacokinetic study, Rat plasma

BACKGROUND

Cystic fibrosis, a progressive genetic disease, induces chronic lung infections and reduces breathing capacity over time.[1] Cystic fibrosis is caused by variations in the transmembrane conductance regulator (cystic fibrosis transmembrane regulator [C.F.T.R]) gene for cystic fibrosis.

C.F.T.R protein regulator works as an ion channel that controls the volume of liquid on the epithelial surfaces by inhibiting sodium absorption and chloride secretion,[2] resulting in thicker and stickier mucus than usual, which is difficult to remove from the lungs by cough leading to difficulty in breathing and severe lung infections.

Symdeko tablet formulation (labeled claim: 150 mg ivacaftor and 100 mg tezacaftor) was approved by Food and Drug Administration (FDA) in 2018.[3,4] Symdeko tablet is suggested for treating patients (aged 12 or older) with cystic fibrosis, patients with homozygous mutation (F508del), or mutation in the C.F.T.R gene. Ivacaftor [Figure 1] is a chloride channel agonist.[5-7] Tezacaftor [Figure 1] is a corrector of C.F.T.R protein,[8] cumulative effects of ivacaftor, and tezacaftor stimulates the C.F.T.R protein functions on the cell's surface, resulting in increased transport of chloride out of the body.[9-11]

To the best of our literature search, stability indicating RP-HPLC method,[12,13] UPLC[14] and UV spectrophotometric methods[15] were published to quantify tezacaftor and ivacaftor simultaneously in tablet formulations. For most of the analytes, liquid chromatography with mass spectrometry is considered as the most sensitive and specific approach compared to all other techniques. Liquid chromatography with mass spectrometry becomes the first option of quantitation for drugs in biological matrices. Three LC-M.S methods have been

Original Article

Thai Journal of Pharmaceutical Sciences

Inhibitory effects of *Manosa alliacea* in Freund's adjuvant arthritis on inflammatory markers and its confirmation by *In-silico* strategy

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ABSTRACT

For the assessment of the curative effect of *Manosa alliacea* on Freud's adjuvant (FA) arthritis on Swiss albino rats. Methanol extract from *M. alliacea* (MEMA) was administered orally at 200 mg/kg and 400 mg/kg, 28 days after FA immunization. For control and treatment groups, paw volume, body weight, hematological parameters, X-ray, and histological tests were measured. In addition, reverse transcription-polymerase chain reaction (RT-PCR) was used to measure the levels of various inflammatory markers. *In vitro*, DPPH and H_2O_2 tests were used to evaluate the antioxidant capability. MEMA decreased paw volume and paw thickness, bodyweight considerably ($P < 0.05, 0.01, 0.001$), compared to hematological anomalies of arthritis control. X- rays tests and histological tests did not reveal significant structural changes in the rat ankle joints administered with MEMA. The levels of expression tumor necrosis factor - α, NF-Kβ, IL-1β, and COX-2 were significantly suppressed in the treatment groups. The *in-silico* study has shown that a number of chemical components in the plants under study can effectively bind to various inflammatory targets. That is why we say *M. alliacea* is a good source for treating rheumatoid arthritis.

Keywords: *Manosa alliacea, In silico, In vivo,* Freund's adjuvant arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, paralytic joint disease that affects 1% of the adult population worldwide.[1] This results in a significant loss of quality of life and the resulting degradation that has a significant socio-economic impact.[2,3] An inflammatory reaction to synovial membrane inflammation, joint lining, which is typically made up of macrophage, and fibroblast-like cells, was activated and called synoviocytes.[4] Free radicals, in particular reactive oxygen species (ROS), also involve RA pathogenesis and cause cartilage destruction either through a direct degradation of the matrix or through activation of the matrix metalloproteinase (MMP).[5]

The most common forms of RA are under the category of Inflammatory immune arthritis (IIA).[6] The cytokines, proteinases, oxygen derivatives, and interleukins (ILs) are inflammatory mediators found in the blood plasma

Original Article

Thai Journal of Pharmaceutical Sciences

Inhibitory effects of *Manosa alliacea* in Freund's adjuvant arthritis on inflammatory markers and its confirmation by *In-silico* strategy

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ABSTRACT

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INTRODUCTION

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The most common forms of RA are under the category of Inflammatory immune arthritis (IIA).[6] The cytokines, proteinases, oxygen derivatives, and interleukins (IL's) are inflammatory mediators found in the blood plasma

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In-silico strategies of some selected phytoconstituents from *Melissa officinalis* as SARS CoV-2 main protease and spike protein (COVID-19) inhibitors

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ABSTRACT

Melissa officinalis (Lamiaceae) was used to treat multiple human afflictions. Literary works demonstrated that it has many biological activities. Today's research aims to recognise *Melissa officinalis* phyto-derived anti-viral compounds against main protease and spike protein of COVID-19, to gain insight into the molecular interactions. In the current study, 12 molecules taken from *Melissa officinalis* were analysed through docking, which is derived from the PubMed database. Docking experiments were conducted with Autodock tool. AdmetSAR and Data warrior servers were eventually used for drug-like prediction. Our research shows that three phytoconstituents from *Melissa officinalis*, namely, Luteolin-7-glucoside-3′-glucuronide, Melitric acid-A and Quadranoside-III have exhibited better binding affinity and stability with the targets of COVID-19 main protease and spike protein. The identified substances can be further extended for *in vitro* and *in vivo* studies to assess their effectiveness against COVID-19.

ARTICLE HISTORY
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KEYWORDS
Melissa officinalis; ADMET; Autodock; Physico-chemical; PASS analysis

1. Introduction

WHO has currently stated an emergency condition due to pandemic coronavirus (COVID-19) that has proactively propagating around the entire world. The virus SARS-CoV-2 can easily trigger signs and symptoms such as high temperature, coughing, pneumonia, queasiness, as well as exhaustion [1,2]. Exact origin of the preliminary transmission to human beings is still unidentified. Presently, there are >100 total genome patterns recognised in the NCBI GenBank, coming from over 10 nations [3]. The variant in between these series is much less than 1%. SARS-CoV-2 has been identified as β-coronavirus which causes severe respiratory tract infection in humans by utilising angiotensin-converting enzyme-2 (ACE2) receptors to infect humans [3]. Chinese experts separated SARS-CoV-2 and also sequenced the genome SARS-CoV-2 on 7 January 2020 [4]. The Main protease (Mpro) is an essential protein required for proteolytic maturation of the virus [5]. Thus, targeting Mpro has the potential to provide effective treatment against SARS-CoV-2 by inhibition of the viral polypeptide cleavage. Spike protein of virus binds to the tissue membrane layer with a receptor-mediated communication which enables a way to host cell. Also makes it possible for the application of well-known protein designed to rapidly develop a version for medicine breakthrough on this brand-new SARS-CoV-2 [6].

The COVID-19 pandemic triggered by SARS CoV-2 has resulted in substantial rates of morbidity and mortality worldwide. The strategy adopted here was to look for *in silico* potential of phyto-constituents against SARS-COV-2 by computational protocols against spike glycoprotein as well as main protease. On the other hand, plants have been essential to human welfare for their uses as therapeutics since ancient times [7,8]. A significant amount of antiviral compounds produced from numerous kinds of plants have been used in many studies [9–11]. Researchers across the globe are screening therapeutic molecules from existing antiviral plant secondary metabolites and are also trying to find novel compounds from medicinal plants to avert this pandemic crisis [12]. *In-silico* based testing has been confirmed to be a handy tool to overcome the obstacles of drug discovery. These computational strategies conserve information in terms of money and time [13–16]. Screening from existing plant metabolites, researchers have been trying to identify and optimise novel compounds from medicinal plants to prevent numerous diseases, including COVID-19.

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Research Article

STABILITY INDICATING RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF ONDANSETRON IN BULK AND THEIR PHARMACEUTICAL DOSAGE FORM

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Keywords: Ondansetron, Validation, HPLC, Dosage Form.

ABSTRACT

A simple, rapid, precise and accurate stability indicating RP-HPLC method was developed and validated for the estimation of Ondansetron in bulk drug and pharmaceutical dosage form. A Phenomenex C18 (150 mm × 4.6 mm I.D., 5 µm particle size) column was used as stationary phase with mobile phase consisting of 0.1% Formic acid (pH 4.25):Acetonitrile in the ratio of 50:50 V/V. The flow rate was maintained at 0.6 mL/min and effluents was monitored at 250 nm. The retention time was 2.91 min. The linearity of the method was observed in the concentration range of 5-25 µg/mL with correlation coefficient of 0.999. The method developed was validated for linearity, precision, accuracy, system suitability and forced degradation studies like acidic, alkaline, oxidative and hydrolytic stress conditions were performed as per ICH guidelines. The results obtained in the study were within the acceptable limits and hence this method can be used for the estimation of Ondansetron in pure drug and pharmaceutical dosage form.

INTRODUCTION

Ondansetron (Figure 1) is a competitive serotonin type 3 receptor antagonist. It is effective in the treatment of nausea and vomiting [1-3]. Chemically it is 9-methyl-3-[(2-methyl-1*H*-imidazol-1-yl)methyl]-2,3,4,9-tetrahydro-1*H*-carbazol-4-one. Ondansetron is a selective antagonist of the serotonin receptor subtype, 5-HT_3. Cytotoxic chemotherapy and radiotherapy are associated with the release of serotonin (5-HT) from enterochromaffin cells of the small intestine, presumably initiating a vomiting reflex through stimulation of 5-HT_3 receptors located on vagal afferents [4]. Ondansetron may block the initiation of this reflex. Activation of vagal afferents may also cause a central release of serotonin from the chemoreceptor trigger zone of the area postrema, located on the floor of the fourth ventricle [5-6].

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Literature survey revealed that few HPLC methods [7-14] were reported for the estimation of Ondansetron. Hence a novel, new, sensitive, specific, accurate and precise HPLC method was developed and validated as per ICH guidelines [15-16] for the estimation of Ondansetron in bulk drug and pharmaceutical dosage form.

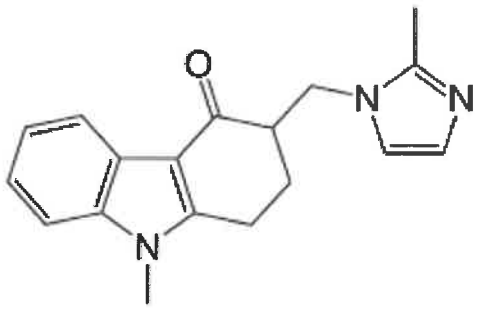

Fig. 1: Chemical structure of Ondansetron

MATERIALS AND METHODS

Instrumentation: To develop a high pressure liquid chromatographic method for estimation of Ondansetron using Agilent Technologies 1260

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International Journal of Research in AYUSH and Pharmaceutical Sciences

Research Article

SIMULTANEOUS ESTIMATION OF METFORMIN AND TENELIGLIPTIN IN PHARMACEUTICAL FORMULATION BY USING UV SPECTROSCOPY

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Keywords: Metformin, Teneligliptin, Wavelength, Validation.

ABSTRACT

Three new UV spectrophotometric methods namely simultaneous equation, absorbance ratio and dual wavelength methods were developed and validated for simultaneous estimation of Metformin and Teneligliptin in bulk drug and tablet formulation which were simple, rapid, sensitive, precise and accurate. In simultaneous equation method, absorbance was measured at 233nm for Metformin and 241nm for Teneligliptin. In absorbance ratio method, absorbance was measured at 244nm for Metformin and 233nm for Teneligliptin. In dual wavelength method, two wavelengths were selected for each drug, the absorbances was measured at 225 and 251nm for Metformin and 240 and 221nm for Teneligliptin. Developed methods were validated according to ICH guidelines including parameters viz., specificity, linearity and range, precision, accuracy, limit of detection and limit of quantification. All the three methods showed linear response in the concentration range of 2-10µg/mL for Metformin and 0.5-2.5µg/mL for Teneligliptin with a low correlation coefficient. Results of method validation parameters follows ICH guideline acceptable limits. Methods were found to be simple, rapid, sensitive, economical and hence can be useful for simultaneous estimation of Metformin and Teneligliptin in pure drug and commercial tablet formulation for routine quality control analysis.

INTRODUCTION

Metformin (MET) (Figure 1) is an oral anti-diabetic drug in the biguanide class. It is the first-line drug of choice for the treatment of type 2 diabetes mellitus[1]. Chemically it is 1-carbamimidamido-N, N-dimethylmethanimidamide. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.[2-3]

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Teneligliptin (TEN) (Figure 2) is a pharmaceutical drug for the treatment of type 2 diabetes mellitus[4]. It belongs to the class of anti-diabetic drugs known as dipeptidyl peptidase-4 inhibitors. Chemically it is [(2S,4S)-4-[4-(5-methyl-2-phenylpyrazol-3-yl) piperazin-1-yl]pyrrolidin-2-yl]-(1,3-thiazolidin-3-yl) methanone. Teneligliptin inhibits the enzyme dipeptidyl peptidase-4 (DPP4) which degrades incretin, a hormone adjusting blood glucose control[5,6].

Literature review revealed that few analytical methods have been reported for the simultaneous determination of Metformin and Teneligliptin in combined pharmaceutical dosage forms using spectrophotometry [7-12]. Hence the objective of the present work is to develop a new, simple, sensitive, specific, precise and accurate UV Spectrophotometric

WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES

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FORMULATION AND EVALUATION OF PARACETAMOL SUSPENSION BY USING NATURAL SUSPENDING AGENT EXTRACTED FROM PEDALIUM MUREX SEEDS

M. Sai Vishnu*, A. Lakshmana Rao, T. Divya Sree, T. Mounika, T. Navya Sri and T. Vineela

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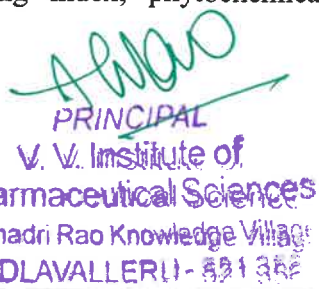
ABSTRACT

The present work was aimed to formulate and evaluate a new, cheap and effective natural suspending agent that can be used as an effective alternative for traditional suspending agent. The study procedure involved extraction of suspending agent from the *Pedalium murex* seeds, determination of swelling index, phytochemical testing, Micromeritic properties of mucilage like Bulk density, Tapped density, Carr's index, Angle of repose, Calibration of paracetamol, preparation of paracetamol suspensions and evaluated for P^H determination, determination of sedimentation volume, redispersibility, determination of flow rate, measurement of viscosity, effect of temperature, drug content, particle size determination and *In-vitro* dissolution studies. The study showed that the extraction of suspending agent from *Pedalium murex* seeds. The swelling index was found to be 60% in distilled water, 40% in 0.1N hydrochloric acid and 30% in phosphate buffer pH 7.4. The photochemical test showed contains carbohydrates. As the concentration of suspending agent increases therefore viscosity of suspension increases which ultimately reduces the sedimentation of suspension.

KEYWORDS: *Pedalium murex,* paracetamol, swelling index, phytochemical testing, Micromeritic properties, sedimentation volume.



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KEYWORDS: *Pedalium murex,* paracetamol, swelling index, phytochemical testing, Micromeritic properties, sedimentation volume.

Asian Journal of Medicine and Health Sciences Vol 4 Supplement 1 October 2021

ORIGINAL ARTICLE

DEVELOPMENT AND VALIDATION OF AN LC-MS/MS METHOD FOR DETERMINATION OF ATORVASTATIN IN HUMAN PLASMA.

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Abstract
Background: A novel method for the estimation of Atorvastatin in human plasma by using LC-MS/MS and the analyte is Atorvastatin and internal standard is Rosuvastatin have extracted with the tertbutyl methyl ether: n-hexane (70:30, v/v) from human plasma.
Methods: The chromatographic severance was attained of the peak using Agilent Zorbax Eclipse XDB-C_8, (100 mm X 4.6 mm, 3.5 µm) column with a run time is 2.5 min. Atorvastatin and Rosuvastatin were recorded at the total ion current of their relevant multiple reaction monitoring. The LC-MS/MS system composed an Agilent 1100 infinity combined with an AB Sciex Qtrap4000 Thermo Finnigan TSQ quantum discovery triple quadrupole mass spectrometer. All of the parameters must be validated like selectivity, accuracy, precision, linearity, lower limit of quantification, matrix effect, recovery reached the acceptance criteria under the following ICH guidelines.
Results: Atorvastatin has checked the various stability studies like short-term stability at 25 °C, long-term stability for 55 days at -70°C, wet extract stability for 54 hours, autosampler stability for 63 hours, benchtop stability for 14 hours and, freeze-thaw stability at -60 °C. Hence, it can be used for routine drug analysis and bioequivalence studies of Atorvastatin in human plasma samples.
Conclusion: The proposed LC-MS/MS method was simple, rapid, precise and accurate for the determination of Atorvastatin in human plasma. The developed LC-MS/MS method can apply for the bioequivalence and pharmacokinetic studies of Atorvastatin in human plasma samples.

Keywords: Atorvastatin, rosuvastatin, estimation, human plasma, LC-MS/MS and validation.

Satya Venkata Sakuntala *et al.*
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Future Journal of Pharmaceutical Sciences

RESEARCH Open Access

Stability-indicating method development and validation for the concurrent determination of darunavir, cobicistat, emtricitabine and tenofovir alafenamide by UPLC in bulk and tablet dosage forms

M. Satya Venkata Sakuntala[1,2*], A. Lakshmana Rao[3] and M. William Carey[4]

Abstract

Background: Tablet dosage forms containing combination of darunavir a protease inhibitor, cobicistat a cytochrome P450 3A inhibitor, emtricitabine and tenofovir alafenamide which were nucleoside reverse transcriptase inhibitors were approved by USFDA on 1st July 2018 to suppress the viral load in HIV patients. It can be used as a complete regimen for the treatment of HIV-1 infection in adults and paediatric patients weighing at least 40 kg. An UPLC method was developed, and separation was done on SB C_8 column of dimensions 50 × 2.1 × 1.8 µ with mobile phase 0.01 N potassium dihydrogen ortho phosphate (p^H-4.8) and acetonitrile in 60:40 ratio, at a flow rate of 0.3 mL/min and an injection volume of 2 µL. The column temperature was maintained at 30 °C, and detection wavelength was 267 nm. The method was validated according to ICH guidelines.

Results: The retention times were 1.031, 1.341, 1.630 and 2.153 min, and they were linear in the concentration range of 1.25–7.5 µg/mL, 18.75–112.5 µg/mL, 25–150 µg/mL and 100–600 µg/mL for tenofovir alafenamide, cobicistat, emtricitabine and darunavir, respectively. The intraday and interday precisions were found to be within acceptable limits. LOD was found to be 0.06 µg/mL, 0.51 µg/mL, 1.31 µg/mL and 3.01 µg/mL, and LOQ was 0.19 µg/mL, 1.54 µg/mL, 3.96 µg/mL and 9.13 µg/mL for tenofovir alafenamide, cobicistat, emtricitabine and darunavir. The correlation coefficients were found to be more than 0.999, and recovery was more than 99.52% indicating the method was accurate. Forced degradation studies reveal that the drugs are unstable under acidic conditions. The method was simple, accurate, precise, stable and can be analysed in less runtime of 4 min.

Conclusions: The flexibility, accuracy and precision of the developed method ensure its applicability in routine analysis of tablet dosage forms.

Keywords: UPLC, Stability indicating, Tenofovir alafenamide, Cobicistat, Emtricitabine, Darunavir

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Research Article

Bio-Analytical Method Development and Validation for Simultaneous Quantification of Glecaprevir and Pibrentasvir in Rat Plasma by Using RP-HPLC

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Abstract

A novel bio-anlytical method was developed for the simultaneous determination of Glecaprevir and Pibrentasvir in rat plasma by using RP-HPLC method. The chromatographic separation was performed on Xterra RP18, (150 mm × 4.6 mm and 3.5 µm) column using the mobile phase ACN: 0.1% formic acid (50:50 v/v). The internal standard used was Voxilaprevir. Glecaprevir, Pibrentasvir and Voxilaprevir peaks were detected at 2.5 min, 5.2 min and 6.3 min respectively. Linear response was obtained in the range of 0.15 µg/mL-2.25 µg/mL for Glecaprevir and 0.06 µg/mL-0.9 µg/mL for Pibrentasvir. All of the parameters must be validated like selectivity, accuracy, precision, linearity, lower limit of quantification, matrix effect, and recovery reached the acceptance criteria under the following of US FDA guidelines.

Keywords: Glecaprevir; Pibrentasvir; Voxilaprevir; Matrix effect; Recovery

Highlights

(RP-HPLC) Reverse PhaseHigh Performance Liquid Chromatography; (ACN) Acetonitrile; (C) Centigrade; (NS) Non Structural; (UV) Ultra Violet; (CV) Coefficent of Variation; (ISTD) Internal Standard; (LLOQ) Lower Limit of Quantitation; (LOQ) Limit of Quantitation; (HQC) High Quality Control; (MQC) Mid Quality Control; (LQC) Low Quality Control; (RS) Related Substances; (SD) Standard Deviation; (P and A) Precision and Accuracy.

Introduction

Infection with hepatitis C virus (HCV) genotype 3 is associated with higher rates of liver steatosis and achieving sustained virologic response quantifiably reverses its progression in those patients. GT3 has been shown to be an independent predictor of fibrosis progression and is associated with a higher incidence of hepatocellular carcinoma. Thus, effective HCV treatment options are critical for patients with HCV GT3 infection, particularly those with advanced liver disease and/or prior treatment experience. replication (Figure 1). Glecaprevir is chemically known as(3aR,7S,10S,12R,21E,24aR)-7-tert-butyl-N-{(1R,2R)-2¬(-difluoromethyl)-1-[(1-methylcyclopropane-1-sulfonyl) carbamoyl]cyclopropyl}-20,20-difluoro¬5,8-dioxo-2,3,3a ,5,6,7,8,11,12,20,23,24a-dodecahydro-1H,10H-9,12methanocyclopenta[2-8]trioxadiazacyclononadecino[11,12-b] quinoxaline-10¬carboxamide hydrate. Glecaprevir disrupts the intracellular processes of the viral life cycle through inhibiting the NS3/4A protease activity of cleaving downstream junctions of HCV polypeptide and proteolytic processing of mature structural proteins [1-12].

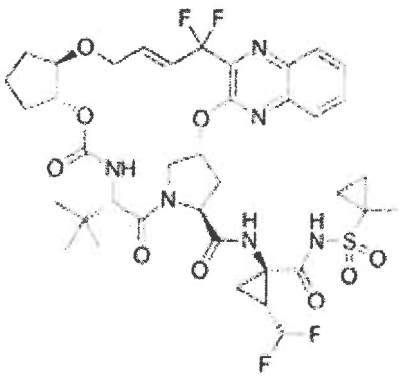

Figure 1: Structure of Glecaprevir.

Pibrentasvir is chemically dimethyl ((2S,2'S,3R,3'R)-((2S,2'S)-(((2R,5R)-1-(3,5-difluoro-4-(4-(4-fluorophenyl) piperidin-1-yl)phenyl)pyrrolidine-2,5-diyl)bis(6-fluoro-1H-benzo[d]imidazole-5,2-diyl))bis(pyrrolidine-2,1-diyl))bis(3-methoxy-1-oxobutane-1,2-diyl))dicarbamate2 (Figure 2). It is a direct acting antiviral agent and Hepatitis C virus (HCV) NS5A inhibitor that targets the viral RNA replication and viron assembly. NS5A is a phosphoprotein that plays an essential role in replication, assembly and maturation of infectious viral proteins. The combination of

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ESTIMATION OF DACLATASVIR IN PHARMACEUTICAL DOSAGE FORM BY ULTRA PERFORMANCE LIQUID CHROMATOGRAPHY

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Keywords:

UPLC, Daclatasvir, Orthophosphoric acid, Acetonitrile

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ABSTRACT: Daclatasvir is an antiviral drug used in combination with other drugs includes sofosbuvir, ribavirin, and interferon, depending on the virus type to treat cirrhosis caused by hepatitis C (HCV). Several methods have been found for quantification, but those are not cost-effective, and they are time-consuming. The present study developed a simple, precise, accurate and cost-effective UPLC method to determine daclatasvir quantity in tablet dosage forms. A simple and selective UPLC method is described for the determination of Daclatasvir Chromatographic separation was achieved on a Acquity BEH C18 (50 × 3.0mm. 1.7 µm) using a mobile phase consisting 0.1% of Orthophosphoric acid: Acetonitrile in a ratio of 60:40 v/v with detection of 248 nm. Linearity was observed in the range 50-150 µg/ml for Daclatasvir (r^2 = 1.000). The amount of drugs estimated by the proposed method was in good agreement with the label claim. The proposed method was validated as per ICH guidelines and applied for the determination of the cited drug in the dosage form.

INTRODUCTION: Daclatasvir is chemically dimethyl N, N'-([1,1'-biphenyl]-4, 4'-diylbis{1H-imidazole-5,2-diyl-[(2S)-pyrrolidine-2,1-diyl][(2S)-3- methyl- 1- oxobutane-1, 2-diyl]}) dicarbamate. Daclatasvir has molecular weight: 738.89 g/mol and molecular formula: $C_{40}H_{50}N_8O_6$. It is an antiviral drug used in combination with other medicaments to treat hepatitis C (HCV). The other medicines used in combination include interferon, sofosbuvir, and ribavirin, depending on the virus type 1. The dose of daclatasvir present in the formulation was determined by using the Ultra Performance Liquid Chromatography method. UPLC has greater sensitivity, resolution, and speed of analysis.

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UPLC operates at high pressure than HPLC, and fine particles, *i.e.*, less than 2.5 µm are used, and mobile phases at high linear velocities decrease the length of the column, reduces solvent consumption, and save time [2].

The UPLC is based on the use of a stationary phase consisting of particles less than 2.5 µm whereas the HPLC column is typically filled with 3-5 µm particles. The principle of this evolution is governed by the Van Deemeter equation, which is an empirical formula that describes the relationship between the linear velocity of flow rate and plate height [3, 4].

$$H = A + B / v + Cv$$

Where; A, B and C are constants, v is the linear velocity, the carrier gas flow rate.

*The A term is independent of velocity and represents "eddy" mixing. It is the smallest when the packed column particles are small and uniform.

Future Journal of Pharmaceutical Sciences

RESEARCH Open Access

Stability-indicating method development and validation for the concurrent determination of darunavir, cobicistat, emtricitabine and tenofovir alafenamide by UPLC in bulk and tablet dosage forms

M. Satya Venkata Sakuntala[1,2*], A. Lakshmana Rao[3] and M. William Carey[4]

Abstract

Background: Tablet dosage forms containing combination of darunavir a protease inhibitor, cobicistat a cytochrome P450 3A inhibitor, emtricitabine and tenofovir alafenamide which were nucleoside reverse transcriptase inhibitors were approved by USFDA on 1st July 2018 to suppress the viral load in HIV patients. It can be used as a complete regimen for the treatment of HIV-1 infection in adults and paediatric patients weighing at least 40 kg. An UPLC method was developed, and separation was done on SB C_8 column of dimensions 50 × 2.1 × 1.8 µ with mobile phase 0.01 N potassium dihydrogen ortho phosphate (p^H-4.8) and acetonitrile in 60:40 ratio, at a flow rate of 0.3 mL/min and an injection volume of 2 µL. The column temperature was maintained at 30 °C, and detection wavelength was 267 nm. The method was validated according to ICH guidelines.

Results: The retention times were 1.031, 1.341, 1.630 and 2.153 min, and they were linear in the concentration range of 1.25–7.5 µg/mL, 18.75–112.5 µg/mL, 25–150 µg/mL and 100–600 µg/mL for tenofovir alafenamide, cobicistat, emtricitabine and darunavir, respectively. The intraday and interday precisions were found to be within acceptable limits. LOD was found to be 0.06 µg/mL, 0.51 µg/mL, 1.31 µg/mL and 3.01 µg/mL, and LOQ was 0.19 µg/mL, 1.54 µg/mL, 3.96 µg/mL and 9.13 µg/mL for tenofovir alafenamide, cobicistat, emtricitabine and darunavir. The correlation coefficients were found to be more than 0.999, and recovery was more than 99.52% indicating the method was accurate. Forced degradation studies reveal that the drugs are unstable under acidic conditions. The method was simple, accurate, precise, stable and can be analysed in less runtime of 4 min.

Conclusions: The flexibility, accuracy and precision of the developed method ensure its applicability in routine analysis of tablet dosage forms.

Keywords: UPLC, Stability indicating, Tenofovir alafenamide, Cobicistat, Emtricitabine, Darunavir

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STABILITY INDICATING HPLC METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF LAMIVUDINE AND DOLUTEGRAVIR IN BULK AND TABLET DOSAGE FORM

Sakuntala Satya Venkata M.[a]*, Lakshmana Rao A.[b] and William Carey M.[c]

(Received 03 April 2020) (Accepted 17 July 2020)

ABSTRACT

A rapid high-performance liquid chromatographic method has been developed and validated for quantification of lamivudine and dolutegravir, used to manage HIV infections. Lamivudine and dolutegravir are separated as symmetrical peaks on the analytical column Inertsil ODS, 150 mm x 4.6 mm, 5.0 µm using 50 % acetonitrile and 50 % triethylamine buffer as mobile phase and detected by photo diode array detector at wave length 250 nm. The total chromatographic runtime is 6.0 min with retention times for lamivudine and dolutegravir at 2.457 and 3.888 min, respectively. The method was validated according to ICH guidelines and linear calibration curves were obtained across a range of 6.01-90.15 µg mL^{-1} and 1.01 -15.15 µg mL^{-1} for lamivudine and dolutegravir, a correlation coefficient of R^2 0.999. Tablets containing lamivudine and dolutegravir were subjected to acid hydrolysis, alkali hydrolysis, oxidising agent, reducing agent, heat and UV light at two variable conditions and the drugs peaks are well resolved. This developed method can be used routinely for the determination of lamivudine and dolutegravir in bulk and tablet dosage form.

Keywords: Lamivudine, dolutegravir, HPLC, stability indicating, ICH guidelines, USFDA

INTRODUCTION

USFDA approved combination of nucleoside reverse transcriptase inhibitor lamivudine and integrase inhibitor dolutegravir for the initial therapy and complete regimen for HIV1 infection in adults in April 2019 and it is marketed under the brand name DOVATO[1].

Lamivudine (Fig.1) is a nucleoside reverse transcriptase inhibitor which acts on HIV1, HIV2 and hepatitis B virus and decreases the chances of developing AIDS. As an inhibitor of reverse transcriptase enzyme, it terminates DNA synthesis. Lamivudine is used to treat hepatitis in lesser dose than for HIV, Chemically, lamivudine is 4-amino-1-[(2*R*, 5*S*)-2-(hydroxyl methyl)-1, 3-oxathiolan-5-yl]-1, 2-dihydro pyrimidin-2-one. Lamivudine is taken along with other antiretrovirals like abacavir and zidovudine. Lamivudine is taken by mouth as liquid or tablet[2, 3].

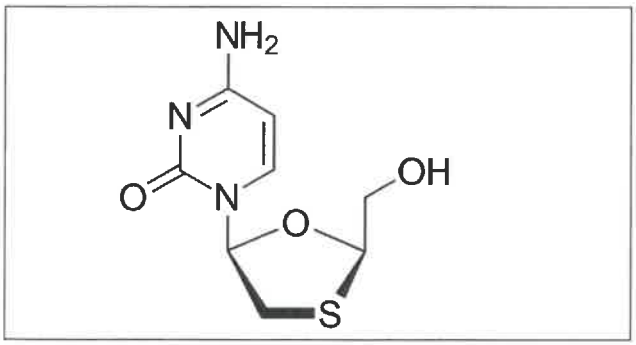

Fig. 1: Structure of lamivudine

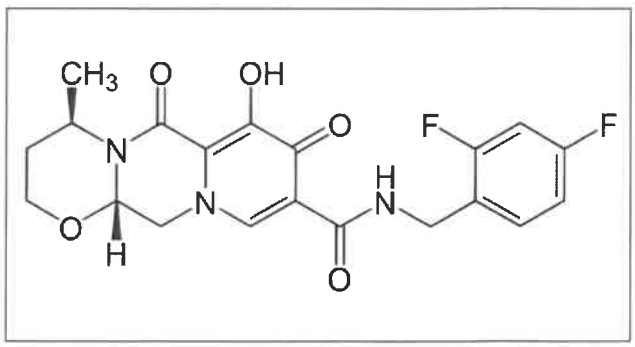

Fig. 2: Structure of dolutegravir

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Research Article

Bio-Analytical Method Development and Validation for Simultaneous Quantification of Glecaprevir and Pibrentasvir in Rat Plasma by Using RP-HPLC

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Abstract

A novel bio-anlytical method was developed for the simultaneous determination of Glecaprevir and Pibrentasvir in rat plasma by using RP-HPLC method. The chromatographic separation was performed on Xterra RP18, (150 mm × 4.6 mm and 3.5 µm) column using the mobile phase ACN: 0.1% formic acid (50:50 v/v). The internal standard used was Voxilaprevir. Glecaprevir, Pibrentasvir and Voxilaprevir peaks were detected at 2.5 min, 5.2 min and 6.3 min respectively. Linear response was obtained in the range of 0.15 µg/mL-2.25 µg/mL for Glecaprevir and 0.06 µg/mL-0.9 µg/mL for Pibrentasvir. All of the parameters must be validated like selectivity, accuracy, precision, linearity, lower limit of quantification, matrix effect, and recovery reached the acceptance criteria under the following of US FDA guidelines.

Keywords: Glecaprevir; Pibrentasvir; Voxilaprevir; Matrix effect; Recovery

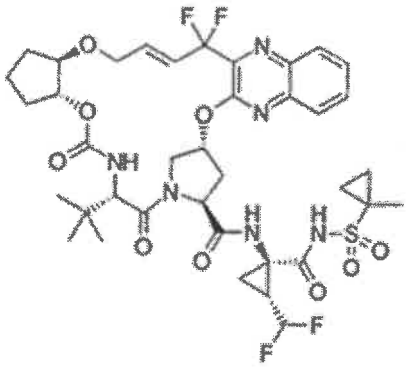
Highlights

(RP-HPLC) Reverse PhaseHigh Performance Liquid Chromatography; (ACN) Acetonitrile; (C) Centigrade; (NS) Non Structural; (UV) Ultra Violet; (CV) Coefficent of Variation; (ISTD) Internal Standard; (LLOQ) Lower Limit of Quantitation; (LOQ) Limit of Quantitation; (HQC) High Quality Control; (MQC) Mid Quality Control; (LQC) Low Quality Control; (RS) Related Substances; (SD) Standard Deviation; (P and A) Precision and Accuracy.

Introduction

Infection with hepatitis C virus (HCV) genotype 3 is associated with higher rates of liver steatosis and achieving sustained virologic response quantifiably reverses its progression in those patients. GT3 has been shown to be an independent predictor of fibrosis progression and is associated with a higher incidence of hepatocellular carcinoma. Thus, effective HCV treatment options are critical for patients with HCV GT3 infection, particularly those with advanced liver disease and/or prior treatment experience.

Glecaprevir is an antiviral agent and Hepatitis C virus NS3/4A protease inhibitor which directly targets the the viral RNA replication (Figure 1). Glecaprevir is chemically known as(3aR,7S,10S,12R,21E,24aR)-7-tert-butyl-N-{(1R,2R)-2¬(-difluoromethyl)-1-[(1-methylcyclopropane-1-sulfonyl) carbamoyl]cyclopropyl}-20,20-difluoro¬5,8-dioxo-2,3,3a ,5,6,7,8,11,12,20,23,24a-dodecahydro-1H,10H-9,12methanocyclopenta[2-8]trioxadiazacyclononadecino[11,12-b] quinoxaline-10¬carboxamide hydrate. Glecaprevir disrupts the intracellular processes of the viral life cycle through inhibiting the NS3/4A protease activity of cleaving downstream junctions of HCV polypeptide and proteolytic processing of mature structural proteins [1-12].



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