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Research Article

Effect of *Lindernia ciliata* (Colsm.) Pennell. against Ethanol Induced Oxidative Damage in HEPG2 Cells

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ABSTRACT

Objective: The study was aimed to assess the in-*vitro* hepatoprotective activity of methanolic extract of whole plant of *Lindernia ciliata* (Colsm.) Pennell. (LCME) of family Scrophulariaceae against ethanol induced cytotoxicity in HepG2 cell lines. Methods: The cytotoxicity study was conducted for the extract, LCME using MTT assay to determine the CTC 50 value. Based on the doses 50, 100 and 200 µg/ml were selected for the hepatoprotective study in HepG2 cell lines. The toxicity was induced by using ethanol (100mM). The in-*vitro* hepatoprotective activity of the extract was assessed based on the changes in the level of biochemical parameters such as Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Lactate dehydrogenase (LDH). Results: The extract, LCME has shown a significant cytoprotective activity with maximum protection and percentage cell viability (69.36%) at 100µg/mL. Conclusion: The study revealed that the extract, LCME has significant in-vitro hepatoprotective activity against ethanol induced cytotoxicity in Hep G2 cell lines.

Key words: Ethanol, HepG2, Hepatoprotective activity, *Lindernia ciliata,* MTT.

INTRODUCTION

Among the various diseases, chronic liver diseases stand one of the serious health problems world wide[1]. Herbal medicines are believed to be much safer and proved elixir in the treatment of various ailments such as diabetes, liver disorders, CNS disorders etc[2]. According to World Health Organization (WHO) about 25% of prescribed drugs worldwide are derived from plants[3]. However, only a small proportion of hepatoprotective plants used in traditional medicine are pharmacologically evaluated for their safety and efficacy and many are yet to be investigated[4].

The plant *Lindernia ciliata* (Colsm.) Pennell. of family Scrophulariaceae is a low growing, stoloniferous, mat-forming, annual, herb from 0.13 - 0.20m high. In India it was found as an insignificant weed, mainly in rice fields[5]. Traditionally it is used as a remedy for gonorrhea, jaundice, urinary disturbances, bronchitis, headache, liver complaints, spleen diseases, constipation, fever, loss of appetite, asthma, cough, skin diseases[6]. There are no reports on the scientific validation of its traditional medicinal claim. In view of this, an attempt has been made in the present investigation to validate its traditional claim in the treatment of liver disorders by using in-*vitro* Hep G2 cell line model which *are* suitable for in-*vitro* model system to study the human liver diseases that are caused by xenobiotic metabolism and other chemicals that cause toxicity to liver[7]. The objective of the present work is to investigate the methanolic extract of whole plant of *Lindernia ciliata* (LCME) for its in-*vitro* hepatoprotective activity against ethanol using HepG2 cell lines.

MATERIALS AND METHODS

Preparation of the plant extract

The whole plant of *Lindernia ciliata* was collected in the month of August 2015, from rice fields of Bayyaram, Warangal district, Telangana state, India, after its authentication by Prof. V.S. Raju, Taxonomist, Kakatiya University, Warangal. The material was washed under tap water and shade dried, coarsely powdered (1 kg) and macerated with methanol in a round bottom flask for 7 days with intermittent stirring and filtered after seven days and concentrated under reduced pressure to yield a dark green semi solid mass. The percentage yield of the extract was found to be 7.4%.

Cell lines, Drugs and Chemicals

HepG2 Cell lines were obtained from National Centre for Cell Sciences (NCCS), Pune India. The drugs and chemicals were purchased from various companies and the details are as follows: Dulbecco's modified eagles medium (DMEM), Silymarin- Sigma Aldrich, Spruce Street, St. Louis, China; Biochemical kits - Merck Specialties Private Limited, Mumbai, India; Fetal bovine serum (FBS) was purchased from Hi-media laboratories, Mumbai, India; Ethanol- Changshu yangyuan chemicals, China. All other chemicals and solvents used were of analytical grade.

Phytochemical analysis

The methanolic extract of *Lindernia ciliata* (LCME), was subjected to chemical tests for detection of various

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Original Article | doi:10.5530/ijper.52.4.69

Quercetin as a Modulator of Diabetic Macrovascular Complications in Murine and Chick Embryo Models

Authors and affiliation (s):

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Department of Pharmaceutical Sciences and Technology, Birla Institute of Technology, Mesra, Ranchi-835215, Jharkand, INDIA.

Abstract:

Background: Quercetin, a bioflavonoid, with wide natural occurrence has been found to possess numerous pharmacological benefits. **Aim:** The present work deals with exploring efficacy of Quercetin against diabetic macrovascular complications taking the aid of the high fat diet fed-low dose streptozotocin rat model. The use of the chick embryo model in this regard was attempted with an aim to address the growing ethical concerns for the use of higher animals in biological experiments. **Methods:** High Fat Diet (HFD) +STZ (35 mg/kg) induced diabetes was treated with metformin and quercetin in rats. Diabetic simulation was done in chick embryos with ß-hydroxy butyric acid (15 mM) and glucose (20 mM). HbA1c, Fasting Blood Glucose (FBG), TC, TG, HDL, LDH and CK-MB were estimated in rat serum whereas blood glucose and lipid profile tests were done in amniotic fluid, liver and heart tissues of chick embryos. Histopathological study was performed on heart tissues of the wistar albino rats. **Results:** Increased HbA1c, blood glucose, TC, TG and decreased HDL were found in the chick embryo models proving its success in simulating diabetic condition. Reversal of blood glucose, HbA1c and lipid profile anomalies towards normal after quercetin treatment was comparable to metformin treated groups in both rat and chick embryo models. Quercetin was found to be effective in decreasing elevated serum LDH and more effective in decreasing CKMB levels. **Conclusion:** Biochemical and histopathological evidences pointed towards quercetin having potential benefits in diabetic macrovascular complications and that the chick embryo is an effective alternative model for the said condition.

Key words: *In ovo*, Diabetic macrovascular complications, Chick embryo, Quercetin.

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METHOD DEVELOPMENT AND VALIDATION BY RP-HPLC FOR SIMULTANEOUS ESTIMATION OF EMTRICITABINE, BICTEGRAVIR, TENOFOVIR ALAFENAMIDE IN FIXED DOSAGE FORM

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[1]Department of Pharmaceutical Chemistry, Sarojini Naidu Vanitha Pharmacy Mahavidyalaya, Affliated to Osmania University,

[2]University College of Technology, Osmania University, Hyderabad.

Abstract:

*Reverse phase HPLC method which is simple, precise, reproducible, accurate was developed for the simultaneous estimation of ETC, BTG, TFRA in fixed combination of formulation drug All the three analytes were separated efficiently using Inertsil 30V C 18 Column (250*4.6mm, 5 micron) using buffer phosphoric dihydrogen phosphate as mobile phase A and methanol and water (70:30) as mobile phase B. Acetonitrile and buffer are used as diluents. The analysis was performed at a wavelength of 265 nm, flow rate of 1.5ml/min and injection volume of 10µl.Linearity was good within the designed concentration range. System suitability was achieved as RSD values were <2. LOD values for ETC, BTG, TFRA were 0.2µg/ml, 0.5µg/ml, 0.0025µg/ml and LOQ values were 0.6µg/ml, 1.5µg/ml, 0.0075µg/ml respectively. Precision and accuracy was achieved as RSD values and percentage recovery was within in the limits i.e., <2 and within 100%. Robustness for the method was achieved using three parameters including pH of the mobile phase, flow rate and different column. In these varied conditions, all three analytes were eluted, resolved and there was no change in their retention times. This proves that this reverse HPLC method developed was simple, accurate, precise and robust for the simultaneous estimation of ETC, BTG, TFRA.*

Key words: *Emtricitabine, bictegravir, tenofovir alafenamide, gradient -HPLC*

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ANTI-TUBERCULAR AND ANTIMICROBIAL ACTIVITIES OF NOVEL HETEROCYCLIC SUBSTITUTED BENZIMIDAZOLE DERIVATIVES

Krishna Veni Chikkula, S. Raja • Published 2018 • Medicine, Chemistry

TLDR From o-phenylenediamine and p-amino benzoic acid a variety of novel heterocyclic substituted benzimidazole analogs C-N were designed and synthesized by a multistep synthesis and exhibited mild to good antitubercular and antimicrobial activity.

Abstract From o-phenylenediamine and p-amino benzoic acid a variety of novel heterocyclic substituted benzimidazole analogs C-N were designed and synthesized by a multistep synthesis. FT-IR, 1H-NMR, Mass spectroscopy and bases of elemental analysis were performed to characterize the structure of synthesized compounds. Test compounds were screened for antitubercular activity against H37RV strains of M. tuberculosis by in vitro M. tuberculosis method. In addition, antimicrobial activity of title compounds was also evaluated against various pathogenic strains of bacteria and fungi by agar streak dilution test. Results of biological studies revealed that all title compounds exhibited mild to good antitubercular and antimicrobial activity. The relationship between the functional group variation and the biological activity of the screened compounds were discussed. The most active compound was found to be 4-(2-(4-(1H-benzmidazol-2-yl)phenyl)hydrazono)-1-(4-chlorophenyl)-3-hydroxy-1H-pyrazol-5(4H)-one H 4-(2-(4-(1H-benzmidazol-2-yl)phenyl)hydrazono)-1-(3-chlorophenyl)-3-hydroxy-1H-pyrazol-5(4H)-one K out of twelve title compounds.
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Figures and Tables

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GASTROPROTECTIVE ACTIVITY OF METHANOLIC EXTRACT OF PHYLLANTHUS ACIDUS FRUIT AGAINST INDOMETHACIN-INDUCED GASTRIC ULCERS IN RATS

Vangala Kavitha, Pathakala Naveen, Ramavath Swathi, Alikatte Kanaka Latha*

This study investigated the gastroprotective effect of methanolic extract of Phyllanthus acidus fruit (MPA) against indomethacin-induced gastric ulcer in rats. Ulceration was induced by a single oral administration of indomethacin (80 mg/kg body weight). Wistar rats were pre-treated with ranitidine (reference drug) at a dose of 40 mg/kg body weight and MPA at doses of 125 and 250 mg/kg body weight once daily for 21 days prior to ulcer induction. After 4 h of indomethacin administration, gastric secretions, antioxidant parameters and stomach nitric oxide (NO) were evaluated. The results showed that indomethacin induced gastric ulcer was associated with a significant increase of malondialdehyde and significant decrease of the gastroprotective mediators such as glutathione (GSH) and NO compared with normal control. Pre-treatment with MPA has shown improvements in indomethacin induced ulcers. In addition, MPA reduced oxidative stress parameters, free and total acidity and gastric NO content. Collectively, MPA produced gastroprotective effect in indomethacin induced gastric ulcers by anti-secretory action and cytoprotective effect. Keywords: Peptic ulcer, indomethacin, glutathione, Phyllanthus acidus, prostaglandins.

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Volume 48, December 2018, Pages 106-117

Antibody-drug conjugates (ADCs): Potent biopharmaceuticals to target solid and hematological cancers- an overview

Naresh Goli [a], Pradeep Kumar Bolla [a b c], Venu Talla [a]

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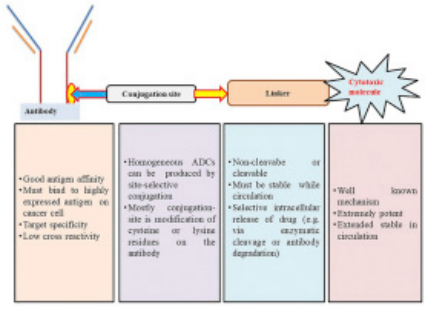
Abstract

Drugs used to target solid and hematological tumors are associated with serious side effects and off-target effects. The non-specificity of classical chemotherapies and radiotherapies leads to poor quality of life in cancer patients. Antibody–drug conjugates (ADCs) are a class of potent immunotherapy-based biopharmaceuticals, which act by intracellular deposit of cytotoxic molecule in antigen positive cancer. ADCs exhibit synergistic activity as it is a combination of monoclonal antibody and small-molecules. It is a linker technology considerably in progress and is currently under research since many years in achieving an extremely selective and magnified therapeutic window. ADC is an inactive pro-drug in bloodstream, activated upon receptor mediated endocytosis into target cancer cell. ADCs contain three elements which include A) suitable monoclonal antibody (mAb) which selectively interacts with over expressed tumor associated target antigens B) cytotoxic drug and C) linker which links cytotoxic drug to mAb by either disulfide/peptide bond. Factors limiting the effectiveness of ADC include reduced cytotoxic drug potency, non-suitable linkers, systemically unstable and less selectivity of mAb towards targeted antigen. This review will discuss in detail on various components of ADC, ADCs under clinical trials, appropriate antigen selection, mechanism, resistance and safety of ADCs along with future prospects.

Graphical abstract



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International Immunopharmacology

Volume 62, September 2018, Pages 191-202

Andrographolide ameliorates silica induced pulmonary fibrosis

Sachin Karkale [a], Amit Khurana [b], Mohd Aslam Saifi [b], Chandraiah Godugu [b], Venu Talla [a]

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https://doi.org/10.1016/j.intimp.2018.07.012

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Highlights

- Andrographolide was found to ameliorate silica induced pulmonary fibrosis.
- Andrographolide intervention significantly reduced BAL fluid parameters.
- Andrographolide potently inhibited silica induced inflammation.
- It inhibits silica induced EMT and ECM deposition.

Abstract

The purpose of this study was to investigate the protective effect of andrographolide in silica-induced pulmonary fibrosis (PF) in mice and its underlying mechanisms. Male Swiss albino mice were divided into five groups: Normal control group, disease control group (1.5 mg silica/60 μL/mice) via oropharyngeal route, low dose (LD) group received silica + andrographolide (3 mg/kg), high dose (HD) group received silica + andrographolide (10 mg/kg), andrographolide per se group received 10 mg/kg andrographolide. Various bronchoalveolar lavage fluid (BALF) and biochemical parameters, inflammatory cytokines, histology and protein expression studies were carried out. Andrographolide significantly reduced total protein concentration, albumin, accumulation of inflammatory cells and lactate dehydrogenase (LDH) level in BALF. We found that andrographolide intervention led to decreased levels of the inflammatory cells including neutrophils, macrophages and lymphocytes in the BALF of the treated animals. In addition, andrographolide significantly reduced nitrite ($p < 0.01$ at HD), malondialdehyde ($p < 0.01$ at HD) and upregulated glutathione ($p < 0.01$ at HD) in silica challenged animals. Andrographolide showed anti-fibrotic activity by reducing collagen deposition and inflammation in lung. Histopathology revealed that andrographolide decreased irregular cellular nodules, inflammatory infiltration and fibrosis. Andrographolide intervention significantly reduced the expression of N-cadherin, α-SMA and vimentin (mesenchymal markers) and upregulated the expression of E-cadherin (an epithelial marker). Hence, andrographolide elicits its anti-pulmonary fibrotic effect by halting the progression of epithelial-to-mesenchymal transition (EMT) via affecting fibroblasts. We, to the best of our knowledge prove for the first time that andrographolide possesses potent antifibrotic activity by targeting inflammatory cells and EMT associated fibroblasts.

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Pulmonary Pharmacology & Therapeutics
Volume 51, August 2018, Pages 32-40

Oropharyngeal administration of silica in Swiss mice: A robust and reproducible model of occupational pulmonary fibrosis

Sachin Karkale [a], Amit Khurana [b], Mohd Aslam Saifi [b], Chandraiah Godugu [b], Venu Talla [a]

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https://doi.org/10.1016/j.pupt.2018.06.003
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Abstract

Pulmonary fibrosis (PF) is a lethal end stage of interstitial lung disease with increasing prevalence. The disease burden of PF has seen a sharp surge in the past two decades owing to entry of heavy amount of particulate matter due to industrialization and urbanization. In this work, we developed an oropharyngeal aspiration model of silica (1.5 mg/mice) induced pulmonary fibrosis as a homogeneous, reproducible, simple and alternative strategy in Swiss albino mice. Various BALF (protein, albumin, cell count), biochemical parameters (MDA, GSH, hydroxyproline), cytokines (IL-1β, IL-6, TNF-α and TGF-β1), histological (H&E and PSR staining) and protein expression (N-cadherin, vimentin, α-SMA, CTGF, collagen-1) studies were conducted to validate the model. Oropharyngeal administration of silica in Swiss mice produced significantly changes in lung morphology with statistically higher lung weights compared to normal control animals. The silica treated mice showed profoundly elevated BALF soluble and cytological parameters and enhanced oxidative and nitrosative stress in lungs. The levels of hydroxyproline were increased by 2.6 fold in the silica treated mice. The expression of pro-inflammatory cytokines were profoundly increased in silica treated mice. The histology and PSR staining indicated increased inflammatory infiltration and staggering fibrosis in silica treated group. In addition, the expression of EMT markers (N-cadherin, vimentin, α-SMA and CTGF) were significantly increased indicating their role in silica induced pulmonary fibrosis. Our work clearly demonstrates the superiority of stress free oropharyngeal instillation of silica with dose reduction over the conventional invasive and non-homogeneous intratracheal route.

Introduction

Pulmonary fibrosis (PF) is a lethal end stage of interstitial lung disease with increasing prevalence [1]. The disease burden of PF has seen a sharp surge in the past two decades due to industrialization and urbanization. This has led to potentially high incidence rate of occupational PF [[2], [3], [4], [5], [6]]. Statistics indicate that there are more than five million PF patients and the incidence rate is in between 0.22 and 7.4%. The disease shows gender bias with higher prevalence among male subjects [[7], [8], [9]]. Silica is a widely used industrial raw material and is cause for PF. The disease can be caused either by long term exposure (>20 years) of low doses of silica or by short term exposure (5–15 years) of high doses of silica [10,11]. Acute exposure of very large doses of silica may lead to inflammation and lung fibrosis. The histological features of the disease indicate scarring of the lung parenchyma, damage to the alveolar cells,

ChemistrySelect / Volume 3, Issue 24 / p. 6766-6774

Full Paper

H_2O-Mediated Epoxide Ring-Opening with Concomitant C–S Bond Formation: A One-Pot Method to 3-Hydroxy-oxindolino-dithiocarbamates as Cytotoxic Agents

Sonal Bhandari, Amol Rajaram Katore, Deepti Madanlal Bajaj, Pankaj Sharma, Dr. Venu Talla, Dr. Nagula Shankaraiah

First published: 25 June 2018

https://doi.org/10.1002/slct.201800983

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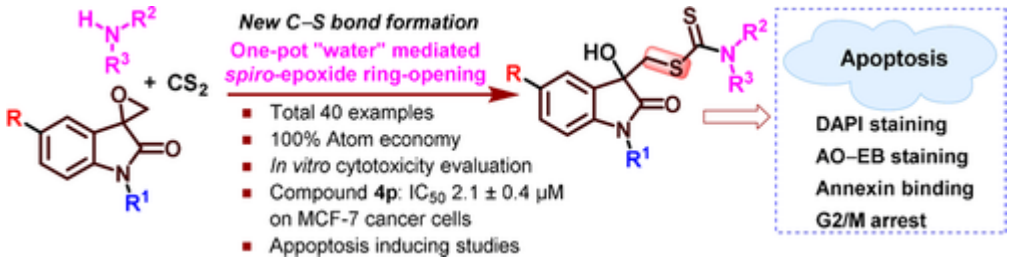
Graphical Abstract

A series of new 3-hydroxy-oxindolino-dithiocarbamate hybrids has been synthesized by a one-pot method and evaluated for their *in vitro* cytotoxicity. Compound **4 p** with a chloro substitution and N-*p*-CN-benzyl on oxindole nucleus displayed potent *in vitro* cytotoxicity against MCF-7 cells with an IC_{50} value of 2.1±0.4 μM. Apoptosis inducing ability and G2/M phase cell cycle arrest on MCF-7 cell line for compound **4 p** was also studied.



Abstract

A simple and efficient one-pot protocol for the synthesis of a library of 3-hydroxy-oxindolino-dithiocarbamate hybrids has been developed and evaluated for their in vitro cytotoxicity potential against selected human cancer cell lines. This one-pot reaction takes place via regiospecific spiro-epoxide ring-opening with concomitant C–S bond formation by an in situ generation of dithiocarbamate intermediate. Gratifyingly, the reaction has been accelerated efficiently in water medium without using any catalyst or

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Research Article

NEW RP-HPLC METHOD FOR THE SIMULTANEOUS ESTIMATION OF PARACETAMOL AND TRAMADOL HYDROCHLORIDE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

The present work was focused on developing a new RP-HPLC method for the simultaneous estimation of paracetamol and tramadol hydrochloride in bulk and tablet dosage form and to validate it as per ICH and USP guidelines. The method involves use of water and acetonitrile in 9:1 ratio as mobile phase pumped at a rate of 1ml/min. The optimum wavelength selected for monitoring was 268nm. C_{18} column (4.6mm×250mm) of 5µ particle size was used as stationary phase. The method was finally validated, and parameters were reported. The system suitability parameters passed in which the asymmetric factors for Paracetamol and Tramadol were 1.54 and 1.09 respectively. Linearity ranges were found to be 20 to 100µg/ml with a correlation coefficient of 0.998. Accuracy studies reported a mean recovery of 98.7% for both the drugs. Faster retention times (1.1min and 4.1min) make the method simple and economic. Thus a validated and sensitive RP-HPLC method was developed for simultaneous estimation of Paracetamol and tramadol in bulk and tablet dosage form.

KEY WORDS: HPLC, Method, Paracetamol, Tramadol hydrochloride, Validation.

INTRODUCTION

Pain is an unpleasant sensation which can lead to distress and discomfort[1]. Pain can be acute or chronic. Drugs used to treat pain are called pain killers or analgesics. Paracetamol and Tramadol are commonly used analgesics. Paracetamol (Figure 1) is chemically N-(4-Hydroxyphenyl)ethanamide or N-(4-Hydroxyphenyl)acetamide. It is a cyclooxygenase-2 (Cox-2) inhibitor and it is used to treat fever and pain. Tramadol (Figure 2) is chemically trans-2-(Dimethylaminomethyl)-1-(m-methoxyphenyl)cyclohexanol. It is an Opioid receptor agonist, 5-HT inhibitor and it is used to treat mild to severe pain, depression. Both paracetamol and tramadol are practically freely soluble in water and methanol[2,3].

Literature survey reveals that much work is documented on the chromatographic (HPLC & HPTLC) estimation of these two drugs in combined pharmaceutical dosage forms[4-17]. However, they are tedious, time consuming and costly. Hence there is a need for the development of a relatively simple, precise, accurate, reproducible and cost effective HPLC method for the estimation of paracetamol and tramadol in tablets and to validate the developed method as per ICH and USP guidelines.

MATERIALS AND METHODS

Instrumentation

The analysis was carried out on a HPLC system (SPINCO BIOTECH) equipped with UV detector. Other apparatus and instruments used were electronic balance (Keroy). Digital pH meter (Systronics). Magnetic stirrer (Remi). Millipore (Direct Q UV3). Ultra sonicator (Pci). Micro pipette (Physio care). Membrane filters (Sartorins). UV- Spectro photometer (Shimadzu UV 1800) (Toshvin). Pipettes and volumetric flasks (Borosil). All instruments and glass-wares were calibrated

Materials

API of Paracetamol was obtained from MSN labs and Tramadol hydrochloride was obtained from NEQ Pvt. Ltd. Tablets (ULTRACET) were purchased from Local market. All chemicals and reagents used were of AR grade.

Chromatographic Conditions

The mobile phase consisted of water and acetonitrile. The chromatograph was operated in the isocratic mode starting at a mobile phase of water: acetonitrile (90:10 v/v). Eluent was delivered at a flow rate of 1 mL/min. Absorbance was monitored at 268 nm.

Preparation of Mobile Phase

Mix 90ml water and 10ml acetonitrile and degas in ultrasonic water bath for 15 minutes. Filter through 0.2 µ filter under vacuum filtration before injection.

Standard Solution preparation

Accurately weigh and transfer 20 mg each of paracetamol and tramadol hydrochloride standard drugs into a 10ml clean dry volumetric flask, add about 7ml of methanol and sonicate to dissolve it completely and make up the volume to the mark with methanol. From this stock solution, aliquots were transferred in

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Special Issue

Article

Synthesis of New 1,2,3-Triazolo-naphthalimide/phthalimide Conjugates via 'Click' Reaction: DNA Intercalation and Cytotoxic Studies

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Cancer is a complex disease which involves abnormalities of multiple cellular pathways. Current chemotherapeutic drugs are mainly designed to target the DNA and cell division. Therefore, in the present study, we have synthesized a new series of 1,2,3-triazolo-naphthalimide/phthalimide conjugates and evaluated their *in vitro* cytotoxicity against selected human cancer cells. Among the tested compounds, one of them displayed notable cytotoxic activity against A549 lung cancer cells with an IC_{50} (half maximal inhibitory concentration) value of 7.6 ± 0.78 μM. To determine the effect of this compound on cell viability, acridine orange/ethidium bromide (AO/EB) and 4',6-diamidino-2-phenylindole (DAPI) staining studies were performed. These apoptotic features were clearly indicating that the compound inhibited cell proliferation by apoptosis. Further, relative viscosity measurements and molecular docking studies with the most three active compounds indicated that these new compounds bind to DNA by intercalation.

Keywords: naphthalimides, 1,2,3-triazoles, DNA intercalation, click reaction

Introduction

Cancer is considered as one of the lethal diseases worldwide and the incidence of cancer has been rising in major regions of the world with predicted substantive increase to 19.3 million by the year 2025.[1] Although the scientific advances focused on finding exact pathophysiology of the disease and tremendous efforts have been made on highly proliferative tissues, the DNA becomes one of the most promising biological targets to develop antitumor agents.[4] DNA replication has an invaluable role in cancer cell division, hence polycyclic planar molecules such as doxorubicin, acridines, anthraquinones, distamycins, naphthalimides and phenanthrene derivatives are well recognized as DNA targeting antitumor agents.[5]

Naphthalimides are aromatic heterocycles with profound

International Journal of Pharmacy and Natural Medicines

Journal Home Page: www.pharmaresearchlibrary.com/ijpnm

RESEARCH ARTICLE

Phytochemical Screening Anti-Inflammatory activity studies on *Caesalpinia coriaria* leaves

Poteti Karunakar*[1], Madathala Sreekanth[2], S. Amer, B. Venkatesh, H. Ramana

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ABSTRACT

The aim of present research work describes on phytochemical screening anti-inflammatory activity studies on *Caesalpinia coriaria* leaves. *Ceaesalpinia coriaria* commonly known as divi. It possess the many biological activities such as antibacterial, antifungal, anti-oxidant and anti-inflammatory activities. The present research screening on anti-inflammatory activity. It also used in siddha and unani medicines. In experimental investigation *Caesalpina coriaria* plant leaves are collected, dried and powdered. Powdered material was soxhlet extraction with methanol. The phytochemical analysis of methanol extract of *ceasalpinia coriaria* revealed the presence of carbohydrates, glycosides proteins, amino acids, tannins, flavonoids, oils and gums.

Keywords: Caesalpinia coriaria, dividivi, Anti-inflammatory, Soxhlet extraction, Phytochemical analysis, Methanol extract

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CONTENTS

1. Introduction

Inflammation is defined as the local response of living mammalian tissues to injury due to any agent. It is the body's defense reaction in order to eliminate or limit the spread of injurious agent as well as to remove the consequent necrosis cells and tissues. Modern medicines from phyto-constituents have little to offer for alleviation of inflammatory activity. The process of inflammation is necessary in healing wounds. However, uncontrolled and persistent inflammation contributes to the progression of many chronic pathological conditions, such as rheumatoid arthritis, atherosclerosis, psoriasis, inflammatory bowel disease, retinitis, multiple sclerosis etc. It may also be associated with increased risk of cancer.

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Development and Validation of a new UFLC method for the estimation of Chlorhexidine in bulk drug

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ABSTRACT

A simple, sensitive and specific UFLC method was developed to estimate Chlorhexidine in bulk drug. Acetonitrile and Water were used in 60:40 v/v ratio as mobile phase. The flow rate of eluent was fixed at 0.8 mL/min. Absorbance was monitored at λmax of 235 nm. A reverse phase column C18, (250mm x 4.6mm i.d., 5µm) was used as stationary phase. The retention time was found to be 2.99 minutes. The linearity range of Chlorhexidine was found to be 1-6 µg/ml at 235nm wavelength.

KEY WORDS: UFLC, Chlorhexidine, Retention time, Linearity.

1. INTRODUCTION

Chlorhexidine is a biguanide antiseptic. Its chemical name is N, N^1-1, 6-Hexanediylbis [N^1-(4-chlorophenyl) imidodicarbonimidic diamide] and its molecular formula is $C_{22}H_{30}Cl_2N_{10}$ (Figure.1.) (Jeffery, 1989). It has a broad spectrum of activity against different microorganisms. Hence it is widely used in dentistry, human and veterinary medicine (Fiorentino, 2010). Antimicrobial effects of Chlorhexidine are associated with the attraction between the drugs and bacterial cells bearing negative charge, thus disrupting the cell membrane integrity.

Literature survey reveals that several reports have been published on the spectroscopic (UV) (Gurdeep, 1991; Paresh, 2014; Rushikesh, 2016; Tarig, 2017) or chromatographic (HPLC) (Bagdanovska, 2014; Liljana, 2014; Zhesu, 2013; Dave, 2012; Zhang, 2012; Soyseven, 2012; Marco, 2011; Beckett, 2002; Snyder, 1997; Skoog, 1980) estimation of chlorhexidine. However, majority of the reports on HPLC revealed the usage of mobile phase containing buffers and longer retention times. Hence, it is felt worthwhile to develop and validate a new, simple, faster UFLC method to estimate chlorhexidine.

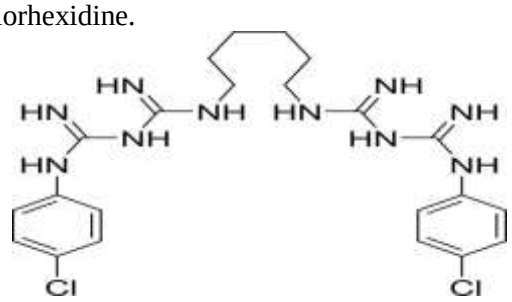

Figure.1. Chemical structure of Chlorohexidine

2. MATERIALS AND METHODS

Instrumentation: UFLC SPD-20A (SHIMADZU), UV-VIS spectrophotometer, UV-1800 (SHIMADZU), Analytical balance AY220 (SHIMADZU), pH meter MK V1 (DIGITAL), Ultra SonicatorPCi (BIOTECHNICS).

Chemicals and reagents: Analytically pure Chlorohexidine was gifted by MSN laboratories. HPLC grade Methanol (HIMEDIA), Acetonitrile (SIGMA ALDRICH), Triethylamine, Ortho phosphoric acid (FINAR) were purchased. Millipore water of HPLC grade was used.

Chromatographic conditions: Glassware used were thoroughly washed using chromic acid cleansing mixture, rinsed with water and dried. Acetonitrile and Water were used in ratio of 60:40 v/v as mobile phase. 0.8 mL/min was fixed as flow rate to deliver the eluent, the run time was 10 minutes and the injection volume was 20µL. Absorbance was monitored at λmax of 235 nm.

Preparation of mobile phase: A mixture of about 400 mL water and 600 mL Acetonitrile (HPLC grade) were mixed and degassed in an ultrasonicator for 5 min. 0.45 µ filter was used to filter the final solution under vacuum. The mobile phase thus prepared was also used as diluent.

Standard Solution Preparation: Standard stock solution of Chlorhexidine was obtained by dissolving 10mg of Chlorhexidine bulk drug in 10ml of methanol to give 1mg/ml of solution (Stock solution). Further dilutions were prepared from the standard stock solution to obtain 1, 2, 3, 4, 5, 6 µg/ml of the solutions.

3. RESULTS AND DISCUSSION

Determination of absorption maxima (λ_{max}): 10µg/ml standard solution of Chlorhexidine was prepared using methanol and scanned in UV Spectrophotometer from 200-400 nm.

Multidrug Resistance Reversal Activity of Some New Dihydropyridines Studied by *IN SITU* Single-Pass Intestinal Perfusion (SPIP) Method in Rat

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Pharmaceutical Chemistry Journal

Aims and scope

K. Sirisha, G. Achaiah, N. Prasad, S. Bhasker, L. Umachander & V. Malla Reddy

3/1/24, 11:48 AM Multidrug Resistance Reversal Activity of Some New Dihydropyridines Studied by IN SITU Single-Pass Intestinal Perfusion (SPIP) Method in Rat | Pharmaceutical Chemistry Journal

P-glycoprotein (P-gp) mediated efflux affects the pharmacokinetics of several drugs. By analogy to verapamil, 1,4-dihydropyridines (DHPs) have been widely studied as P-gp inhibitors. Previously, we have reported on two new DHPs: IA_1(A) and IIA_5(B) as inhibitors of human MRP1, an efflux protein closely related to P-gp. The aim of the present study was to investigate the inhibitory effects of these two compounds on intestinal P-gp using the method of *in situ* single-pass intestinal perfusion (SPIP) in rat. According to this, the intestinal absorption of zidovudine (a P-gp substrate) was studied in anaesthetized rat jejunum in the absence and presence of DHPs IA_1(A) and IIA_5(B) (2 mg/kg). Verapamil (0.8 mg/kg), a well-known P-gp inhibitor, was employed as a standard. Zidovudine solution (200 ig/mL) in phosphate buffer (pH 7.4) was perfused through the jejunal segment, the perfusate concentrations were quantified by HPLC, and the permeability coefficient (P_{eff}) and fraction absorbed (F_{abs}) were calculated. Phenol red was used as a non-absorbable marker to correct water flux through the segment. In rats pretreated with compounds IA_1 and IIA_5, P_{eff} and F_{abs} of zidovudine were found to be 0.1669 ± 0.12 cm/sec, 0.2035 ± 0.18 and 0.2798 ± 0.12 cm/sec, 0.3015 ± 0.14,

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Original Article

NEW VALIDATED METHOD DEVELOPMENT FOR THE ESTIMATION OF SULFAMETHOXAZOLE AND TRIMETHOPRIM IN BULK FORM BY VISIBLE SPECTROSCOPY

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ABSTRACT

Objective: To develop three novel, sensitive, simple validated visible spectrophotometric methods for the quantitative estimation of sulfamethoxazole (SMZ) and trimethoprim (TMP) in bulk form.

Methods: Methods were based on coupling the diazotized aromatic primary amino group of the studied drugs with *o*-phenylenediamine (OPD) in an acidic medium. The first two methods have been proposed for estimation of SMZ and rest for TMP. The resulting products were measured by spectrophotometric (method I, II and III) tools. The methods were validated as per ICH guidelines.

Results: In method I, the absorbance was measured at 482 and 457 nm with linearity ranges of 4.0-40.0 and 5.0-45.0 µg/ml for SMZ. On the other hand, method III was devoted to estimate TMP spectrophotometrically at 457 nm with linearity range of 5-30 µg/ml. The r^2 value for all methods were found to be 0.99. The percentage recoveries of SMZ and TMP were found to be 97.98%, 97.56% and 97.55% respectively. The developed methods were subjected to detailed validation procedure in their pure forms.

Conclusion: The study concludes that visible spectrophotometric validation methods can be very efficient and economically promising technique for the quantitative analysis of SMZ and TMP in bulk form. The statistical analysis of data indicates that the developed methods were reproducible and specific. It was found that there is a good agreement between the obtained results and those obtained by the reported methods; moreover they can be used for the routine estimations of SMZ and TMP in bulk form.

Keywords: Sulfamethoxazole, Trimethoprim, Diazotization, Visible spectrophotometry, Validation

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INTRODUCTION

Sulfonamides are extensively used for the treatment of different bacterial infections in human and veterinary practice [1]. Sulfonamides of pharmaceutical products usually consist, of one sulfonamide mixed with another drug that increases the power of the sulfonamide, e.g. the SMZ and TMP binary mixture. The synergistic antibacterial effect of TMP in combination with sulfonamide is well known both in the *in vitro* and *in vivo* situations [2].

SMZ is chemically 4-amino-N-(5-methylisoxazol-3-yl)-benzene sulfonamide (fig. 1) is a structural analog of para-aminobenzoic acid. Inhibiting the production of dihydrofolate intermediate binding through dihydropteroate synthetase interferes with the normal bacterial synthesis of folic acid, which inhibits the folate-dependent metabolic process for bacterial growth [3].

TMP is designated chemically as 5-(3,4,5-trimethoxy benzyl) pyrimidine-2,4-diamine (fig. 2) which binds dihydrofolate reductase and decrease the levels of tetrahydrofolic acid which an essential precursor in the thymidine synthesis pathway, inhibits bacterial DNA synthesis. TMP affinity for bacterial dihydrofolate reductase is several thousand times greater than its affinity for human dihydrofolate reductase [4].

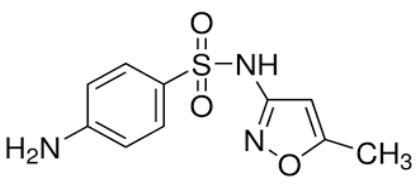

Fig. 1: Structure of SMZ

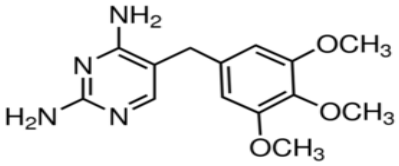

Fig. 2: Structure of TMP

Among the various methods available for the estimation of these drugs in literature survey, such as charge transfer complexation [5], uv-visible spectrophotometry [6-16], square wave voltametry [17], rapid UPLC [18], HPLC [19], chemical evaluation [20], spectroflourimetry [21] and flow injection system/HPLC with potentiometry [22], colorimetric sensors have attracted increasing considerations for their convenience of visual observation and simple operations in recent years [23-25]. OPD and its derivatives have been widely used in the estimation of enzymes and drugs [26, 27].

From literature, hitherto there are no visible spectrophotometric methods reported for the estimation of SMZ and TMP using OPD through diazotization followed by coupling reaction which encouraged us to develop these methods. Hence, for the first time, we describe few simple, sensitive, cost-effective, novel methods using OPD to assay these drugs in bulk samples.

MATERIALS AND METHODS

Apparatus

The visible spectra of drug solutions were recorded on a Shimadzu 1800 UV/Vis spectrophotometer at room temperature in 1 cm quartz cell. The wavelength range was from 200 to 800 nm. For spectral data acquisition and processing UV probe software was used.

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Original Article

EFFECT OF *MOMORDICA CHARANTIA* AND *SYZYGIUM CUMINI* EXTRACT ON SERUM ELECTROLYTES IN ALLOXAN INDUCED DIABETIC RATS

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ABSTRACT

Objective: Diabetes is a group of disorders characterized by high blood glucose levels. Disturbances in serum electrolytes like sodium (Na^+) and potassium (K^+) are found in diabetes. The purpose of the study was to investigate the disturbances in concentrations of serum electrolytes in hyperglycemic crisis and the effect of *syzygium cumini* and *momordica charantia* standardized aqueous extracts on serum electrolytes ($Na^+$and K^+) in normal and diabetic rats.

Methods: Diabetes is induced by intraperitoneal injection of alloxan at a dose of 120 mg/kg b. w in rats. Rats were divided into 5 groups (normal control, disease control, metformin, test 1 and test 2). In test groups 1 and 2, SASESC (standardized aqueous seed extract of *syzygium cumini*) and SAFEMC (standardized aqueous fruit extract of *momordica charantia*) were respectively administered orally to alloxan induced diabetic rats, and their serum electrolyte levels were observed at 1st, 4th, 7th and 14th days.

Results: By the 14thday, the Na^+ and K^+ levels in groups 4 and 5 were almost normal. However, in group 3 (standard), Na^+ levels were relatively lower and K^+ levels were relatively higher than groups 4 and 5 (test). In group 2 (disease control) as compared to group 1 (normal control), a decrease in Na^+ and increase in K^+ levels was observed even on day 14.

Conclusion: Treatment with anti diabetic drugs like metformin, *syzygium cumini* (test-1), *momordica charantia* (test-2) restored the electrolyte levels almost back to normal over a period of study (14 d). There was significant (**P<0.01, *P<0.05) normalization of electrolyte levels in diabetic rats. It was concluded that *syzygium cumini* and *momordica charantia* showed better efficiency in restoring the electrolyte imbalance as compared to metformin during our study.

Keywords: *Syzygium cumini, Momordica charantia,* Metformin, Diabetes, Electrolyte, Alloxan

DOI: http://dx.doi.org/10.22159/ijpps.2018v10i11.24963

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by high blood glucose level (hyperglycemia) resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs like the eyes, kidneys, nerves, heart, and blood vessels [1, 2]. Electrolytes are salts in the body that conduct electricity and are found in fluid, tissue and blood. A proper balance of electrolytes such as sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), magnesium (Mg^{2+}) and others are essential for overall health. They have a pivotal role in the maintenance of homeostasis inside the body, regulation of heart and brain function, body fluid balance, ventilation, pH etc [3]. Deficiency or imbalance of electrolytes can lead to serious conditions. DM is amongst those diseases which show frequent disturbances of electrolytes and acid-base relations, especially in patients with deranged renal function and other end-organ injury, mal-absorption syndromes, acid-base imbalances and multiple drug regimens and medications for DM management. The knowledge and insight of the disease process and its management would create the way for 'pathophysiology-directed therapy', leading to prevention of the several adverse effects associated with acid-base and electrolyte disorders and their management [4-8].

Alterations of ionized Na^+, K^+, and Mg^+ in the serum have been reported in DM subjects, both as causes and consequences. There is also increasing evidence that electrolyte imbalances are early biochemical events responsible for long-term diabetic complications. Considerable variations in the electrolyte metabolism may exist in populations depending on the genetic constitution, nutritional status, and environmental situation. It has been suggested that alterations in Na^+, K^+, Ca^{2+} and other biologically relevant elements might occur due to malfunction of Na^+-K^+ pumps. There is increasing evidence that these alterations of electrolytes across the cell may play a vital role in the mechanism of cellular injury leading to retinopathy, nephropathy, and neuropathy in DM subjects [9]. The present study was chosen to investigate the serum levels of Na^+ and K^+ in alloxan-induced diabetic rats without any complications.

Drugs used to treat DM like metformin and sulfonylureas along with tricyclic antidepressants (used to treat neuropathy) can also cause electrolyte and acid-base disturbances. In modern medicine, no satisfactory effective therapy is available to control DM along with electrolyte imbalance. The literature survey reveals that anti-diabetic herbs have the capacity to cure electrolyte imbalance along with DM [10-13]. In this regard, an herbal anti-diabetic drug used traditionally viz., *momordica charantia* and *syzygium cumini* were chosen for the present study to investigate a possible effect of the standardized aqueous fruit extract of *momordica charantia (*SAFEMC*)* and standardized aqueous seed extract of *syzygium cumini* (SASESC) on the serum electrolytes in alloxan-induced diabetic rats.

MATERIALS AND METHODS

Drugs and chemicals

SAFEMC and SASESC were procured from navachethana kendra Pvt. Ltd, Delhi and Shree narnarayan ayurvedic pharmacy, Ahmedabad, Gujarat, India respectively. Alloxan monohydrate was purchased from Chemit Labaratories, Hyderabad, India. Metformin was purchased from nice chemical Pvt. Ltd, Cochin, and India. The glucose estimation kit was purchased from Vijaya diagnostics; Hanamkonda, India and all other chemicals used in this study were obtained commercially and were of analytical grade.

A CLINICAL STUDY ON THE RELATIONSHIP BETWEEN MATERNAL HEMOGLOBIN AND GESTATIONAL DIABETES MELLITUS IN HYDERABAD POPULATION

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ABSTRACT :
Type 1 Diabetes Mellitus is a metabolic disease where the insulin producing β-cells in the pancreatic islets of Langerhans are progressively destroyed. When the insulin production is no longer sufficient to keep the appropriate blood glucose concentration, hyper glycaemia with subsequent glycosuria occurs. The objective of this study was to determine the relationship between the hemoglobin levels during the first trimester of pregnancy with gestational diabetes incidence in pregnant women. This is an analytical, prospective, cohort study conducted with convenience sampling from December 2017 to March 2018. Sample size was determined as follows: 50 people with a confidence interval of 95%, relative accuracy of 25% and a probability of exclusion of 10%. The Ethics Committee approved for our study. Analysis of the different groups (in terms of hemoglobin levels) did not indicate any significant differences among them regarding the above variables, as well as the type and duration of complement intake in pregnancy (p>0.05). As Table II depicts, 5 (8.2%) of all cases developed gestational diabetes, among which 50 (83.67% of those afflicted) were in the High group (hemoglobin levels of 1.25 and higher). All cases were followed up to the delivery due to developing gestational diabetes and the supplements, duration of intake and their types were recorded on each visit. It appears that hemoglobin level during the first trimester of pregnancy may be considered as a selective screening factor for gestational diabetes.
Keywords: gestational diabetes, confidence interval, probability

I.INTRODUCTION

Diabetes mellitus [1, 2]

Type 1 Diabetes Mellitus is a metabolic disease where the insulin producing β-cells in the pancreatic islets of Langerhans are progressively destroyed. When the insulin production is no longer sufficient to keep the appropriate blood glucose concentration, hyper glycaemia with subsequent glucosuria occurs. Type 1 diabetic patients require exogenous insulin administration in order to restore a normal metabolic state.

Gestational diabetes

Gestational diabetes (or gestational diabetes mellitus, GDM) is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy (especially during their third trimester). GDM usually becomes apparent during the 24th to 28th weeks of pregnancy. It is associated with both impaired insulin secretion and the blocking effects of other hormones on the insulin that is produced, a condition referred to as insulin resistance. Diabetic symptoms usually disappear following delivery.

EPIDEMIOLOGY [2,3,4]

The prevalence of GDM in India varied from 3.8 to 21% in different parts of the country, depending on the geographical locations and diagnostic methods used. GDM has been found to be more prevalent in urban areas than in rural areas. For a given population and ethnicity, the prevalence of GDM corresponds to the prevalence of impaired glucose tolerance (IGT) (in nonpregnant adult) within that given population.

CLASSIFICATION [2, 3]

Diabetes mellitus can occur during pregnancy in 2 forms: pregestational and gestational diabetes. World

ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

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Formulation and evaluation of extended-release tablets of an antidepressant drug Venlafaxine HCl

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Keywords:

Venlafaxine HCl,
HPMC,
Ethylcellulose,
Xanthan gum,
Extended-release tablets

ABSTRACT

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects. A dosage form that allows at least a twofold reduction in dosage frequency as compared to that drug presented as an immediate-release (conventional) dosage form is extended-release dosage form. It includes controlled-release, sustained-release, and long-acting drug products. The mechanism of action of venlafaxine HCl in humans is believed to be associated with its potentiation of neurotransmitter activity in the CNS. Venlafaxine and its active metabolite, O-Desmethylvenlafaxine (ODV), inhibit the reuptake of both serotonin and norepinephrine. In the present work, an attempt has been made to develop extended-release (ER) coated tablets of Venlafaxine HCl by selecting different grades of polymers, Hydroxypropyl methyl cellulose, ethyl cellulose and xanthan gum. These are used as retarding polymers to extend the drug release. All the formulations were prepared by wet granulation method and compressed using 9.8 mm punches on 16 stations rotary tablet punching machine. The blend of all the formulations showed poor flow properties. In order to improve flow, higher % of glidant was used. The coating material used was ethylcellulose aqueous dispersion (Aquacoat ECD 30). The prepared ER coated tablets of Venlafaxine HCl showed good post-compression parameters. They passed all the evaluation tests as per USP limits. Among all the formulations, F7 showed maximum % drug release, i.e., 99 % in 24 hours hence it is considered as optimised formulation. The optimised formulation compared with marketed tablets.

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INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of the different dosage form. The oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost-effective manufacturing process (Ansel, 2004).

Extended-release drug products (Jain, 2008) are dosage form that allows at least a twofold reduction in dosage frequency as compared to that drug presented as an immediate-release dosage form.